FILE COVERS 1907 - 16 Oct 2004 VOL 141 ISS 17
FILE LAST UPDATED: 15 Oct 2004 (20041015/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1 STRUCTURE UPLOADED

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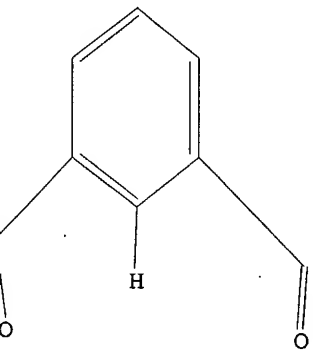
L1 HAS NO ANSWERS
L1 STR




Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
**REGISTRY INITIATED**
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 13:48:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 497633 TO ITERATE

80.4% PROCESSED 400000 ITERATIONS 60742 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.03

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 497633 TO 497633
PROJECTED ANSWERS: 74744 TO 76392

L2 60742 SEA SSS FUL L1

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=> s l3 and py<2001
      20629913 PY<2001
L4        17182 L3 AND PY<2001

=> s l4 and treat?
       3094869 TREAT?
L5         2693 L4 AND TREAT?

=> s l5 and (breast carcinoma or rheumatoid arthritis or osteoarthritis or heart failure)
          56517 BREAST
         115548 CARCINOMA
           5773 BREAST CARCINOMA
                  (BREAST(W)CARCINOMA)
          23701 RHEUMATOID
          34066 ARTHRITIS
          20506 RHEUMATOID ARTHRITIS
                  (RHEUMATOID(W)ARTHRITIS)
           5833 OSTEOARTHRITIS
         294581 HEART
         160480 FAILURE
          16179 HEART FAILURE
                  (HEART(W)FAILURE)
L6           27 L5 AND (BREAST CARCINOMA OR RHEUMATOID ARTHRITIS OR OSTEOARTHRIT
                IS OR HEART FAILURE)

=> d 1-27, ibib abs hitstr

L6   ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2000:881130  CAPLUS
DOCUMENT NUMBER:          134:42124
TITLE:                    Preparation of diaminothiazoles for inhibiting protein
                          kinases
INVENTOR(S):              Chu, Shao Song; Alegria, Larry Andrew; Bender, Steven
                          Lee; Benedict, Suzanne Pritchett; Borchardt, Allen J.;
                          Kania, Robert Steve; Nambu, Mitchell David;
                          Tempczyk-Russell, Anna Maria; Sarshar, Sepehr
PATENT ASSIGNEE(S):       Agouron Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 397 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     WO 2000075120         A1    20001214    WO 2000-US15188          20000602 <--
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             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
             CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1181283            A1    20020227    EP 2000-942660           20000602
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     BR 2000011585         A     20020319    BR 2000-11585            20000602
     JP 2003501420         T2    20030114    JP 2001-501601           20000602
     EE 200100659          A     20030217    EE 2001-659              20000602
     US 2002025976         A1    20020228    US 2001-783584           20010215
     US 6620828            B2    20030916
     ZA 2001008291         A     20021009    ZA 2001-8291             20011009
     NO 2001005045         A     20020204    NO 2001-5045             20011017
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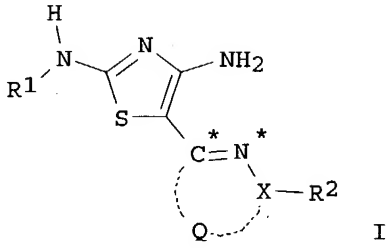
BG 106276 A 20021031 BG 2002-106276 20020103
PRIORITY APPLN. INFO.: US 1999-137810P P 19990604
US 2000-587530 B1 20000602
WO 2000-US15188 W 20000602
OTHER SOURCE(S): MARPAT 134:42124
GI



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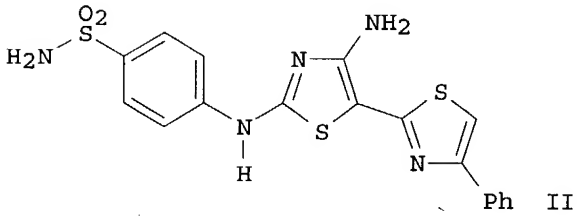


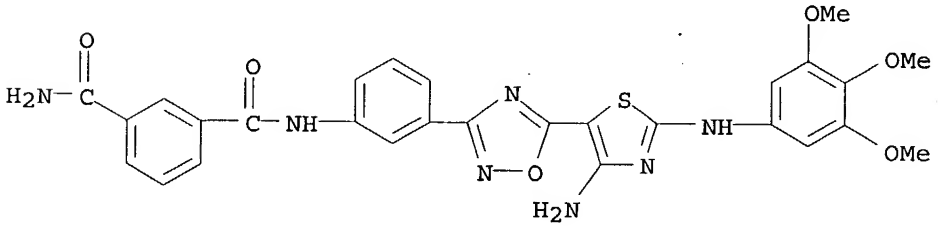
II

AB The title compds. [I; R1 = H, (un)substituted alkyl, cycloalkyl, etc.; R2 = OH, halo, CN, etc.; X = C, N; Q = a divalent radical having 2 or 3 atoms selected from C, N, O, S, CR5, NR5 (wherein R5 = OH, halo, CN, etc.) which together with C* and N* form a 5-6 membered (non)aromatic ring] which modulate and/or inhibit the activity of certain protein kinases (biol. data were given), and are useful in **treating** cancer as well as other disease states associated with unwanted angiogenesis and/or cellular proliferation, such as diabetic retinopathy, neovascular glaucoma, **rheumatoid arthritis**, and psoriasis, were prepared and formulated. E.g., a multi-step synthesis of diaminothiazole II was given. The compds. I and pharmaceutical compns. containing them are capable of mediating tyrosine kinase signal transduction in order to modulate and/or inhibit unwanted cell proliferation.

IT **312763-38-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diaminothiazoles for inhibiting protein kinases)

RN 312763-38-5 CAPLUS

CN 1,3-Benzenedicarboxamide, N-[3-[5-[4-amino-2-[(3,4,5-trimethoxyphenyl)amino]-5-thiazolyl]-1,2,4-oxadiazol-3-yl]phenyl]- (9CI) (CA INDEX NAME)

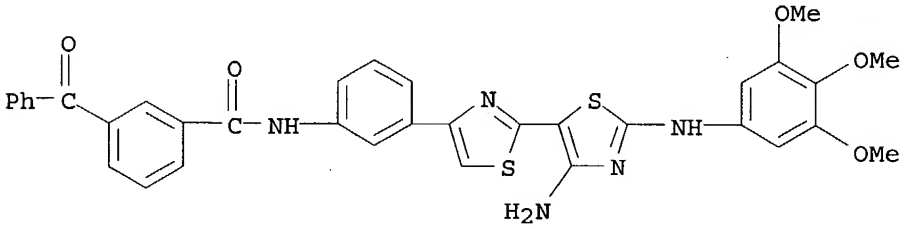


IT **312769-34-9 312770-65-3 312770-77-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of diaminothiazoles for inhibiting protein kinases)

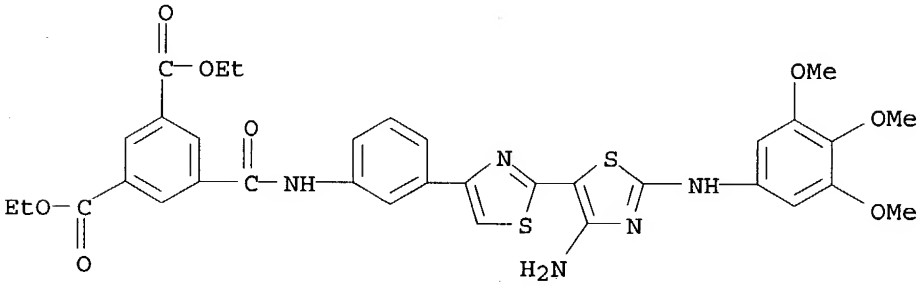
RN 312769-34-9 CAPLUS

CN Benzamide, N-[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]-3-benzoyl- (9CI) (CA INDEX NAME)



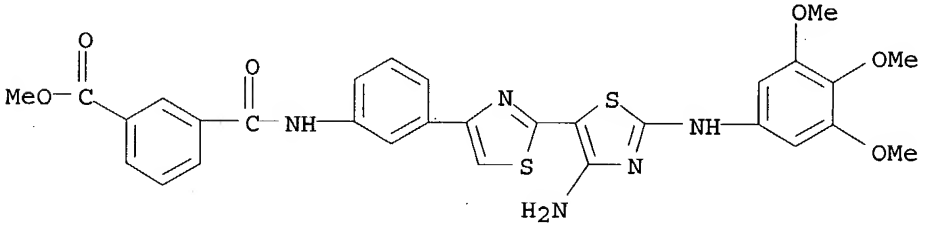
RN 312770-65-3 CAPLUS

CN 1,3-Benzenedicarboxylic acid, 5-[[[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]amino]carbonyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 312770-77-7 CAPLUS

CN Benzoic acid, 3-[[[3-[4'-amino-2'-[(3,4,5-trimethoxyphenyl)amino][2,5'-bithiazol]-4-yl]phenyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:824101 CAPLUS

DOCUMENT NUMBER: 134:5154

TITLE: Preparation of cyclic amine derivatives as remedies or preventives for diseases in association with chemokines or chemokine receptors

INVENTOR(S): Shiota, Tatsuki; Miyagi, Fuminori; Kamimura, Takashi; Ohta, Tomohiro; Takano, Yasuhiro; Horiuchi, Hideki

PATENT ASSIGNEE(S): Teijin Limited, Japan

SOURCE: PCT Int. Appl., 405 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000069432 | A1 | 20001123 | WO 2000-JP3203 | 20000518 <-- |
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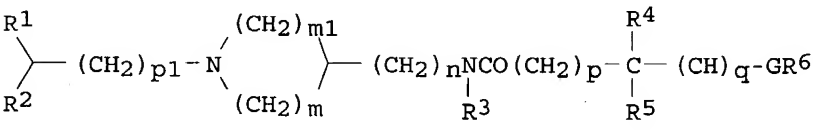
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1179341 | A1 | 20020213 | EP 2000-927808 | 20000518 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| NZ 515374 | A | 20040924 | NZ 2000-515374 | 20000518 |
| NO 2001005599 | A | 20011116 | NO 2001-5599 | 20011116 |
| PRIORITY APPLN. INFO.: | | | JP 1999-175856 A | 19990518 |
| | | | JP 1999-251464 A | 19990906 |
| | | | WO 2000-JP3203 W | 20000518 |

OTHER SOURCE(S): MARPAT 134:5154

GI



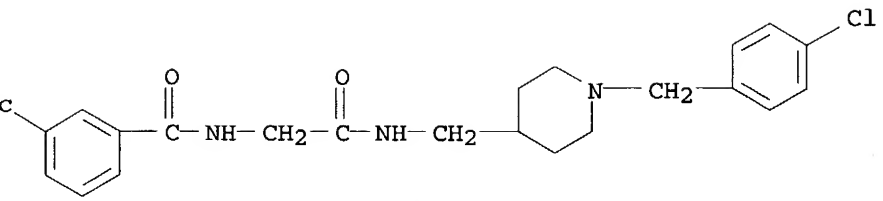
I


AB Remedies or preventives for diseases in association with chemokines such as MIP-1α and/or MCP-1 or chemokine receptors such as CCR1 or CCR2 contain as the active ingredient N-acyl-amino acid N-cyclic amino or N-cyclic aminoalkyl-amide derivs. represented by general formula [I; (un)substituted Ph, C3-8 cycloalkyl, aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N; R2 = H, (un)substituted C1-6 alkyl, C2-7 alkoxycarbonyl, HO, (un)substituted Ph; p1, m1 = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted C1-6 alkyl; R4, R5 = H, OH, (un)substituted Ph or C1-6 alkyl; or R4 and R5 are combined together to form a 3- to 5-membered hydrocarbyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NR7SO2, or SO2NR7, NHCONH, NHCSNH, NH CO2, O2CNH; R7 = H, C1-6 alkyl; or R7 and R5 are combined together to form C2-5 alkylene; R6 = (un)substituted Ph, C3-8 cycloalkyl, C3-6 cycloalkenyl, CH2Ph, or aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N, wherein Ph, CH2Ph, or aromatic heterocyclyl group is optionally fused with (un)substituted benzene or aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S, and/or N], pharmaceutically acceptable acid-adducts thereof, or pharmaceutically acceptable C1-6 alkyl-adducts thereof. The above diseases include destruction of bone or cartilage (e.g. arthritis, **rheumatoid arthritis**, **osteoarthritis**, osteoporosis, injury, and tumor), nephritis, kidney diseases, glomerulus or interstitial nephritis, nephrotic syndrome, demyelinating disease, or multiple sclerosis. Thus, N-3-ethoxybenzyl-D-methionine-N-[1-(4-chlorobenzyl)-4-piperazinylmethyl]amide in vitro inhibited the binding of human MIP-1α to THP-1 cells by >80% at 2 μM.

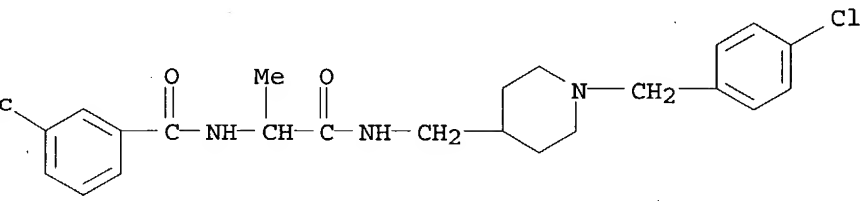

IT **226231-26-1P 226232-13-9P 226232-44-6P**
**226232-66-2P 226232-70-8P 226233-64-3P**
**226233-91-6P 226241-34-5P 226241-35-6P**
**226241-39-0P 226241-41-4P 308360-90-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic amine derivs. as remedies or preventives for diseases in association with chemokines or chemokine receptors)

RN 226231-26-1 CAPLUS

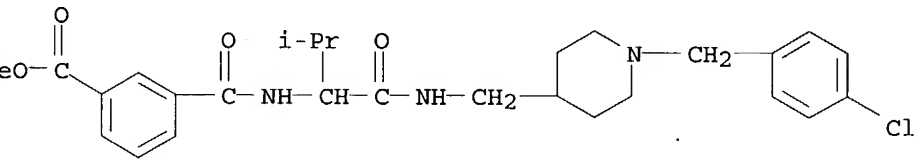
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



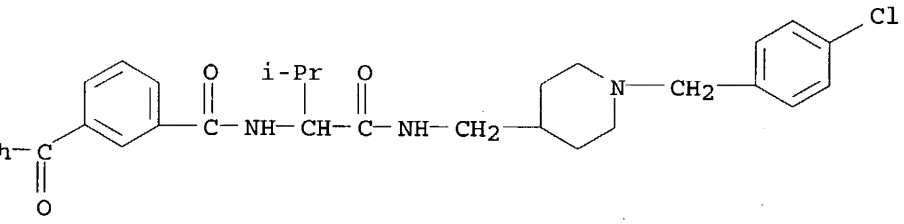
N 226232-13-9 CAPLUS
N Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)



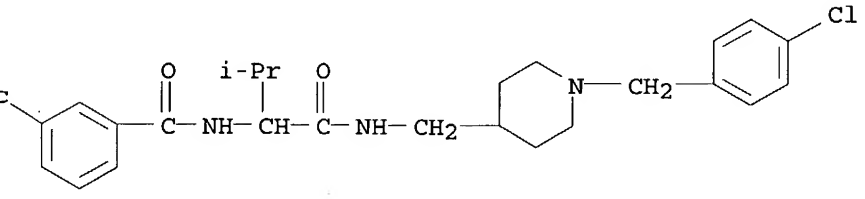
N 226232-44-6 CAPLUS
N Benzoic acid, 3-[[[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



N 226232-66-2 CAPLUS
N Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

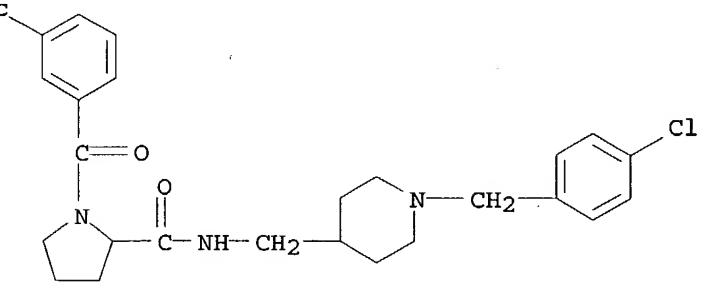


N 226232-70-8 CAPLUS
N Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)

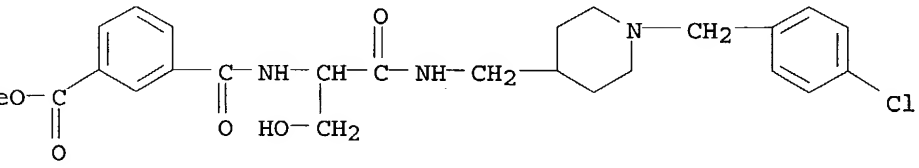


N 226233-64-3 CAPLUS

N 2-Pyrrolidinecarboxamide, 1-(3-acetylbenzoyl)-N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



N 226233-91-6 CAPLUS
N Benzoic acid, 3-[[[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-(hydroxymethyl)-2-oxoethyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



N 226241-34-5 CAPLUS
N Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-chlorophenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

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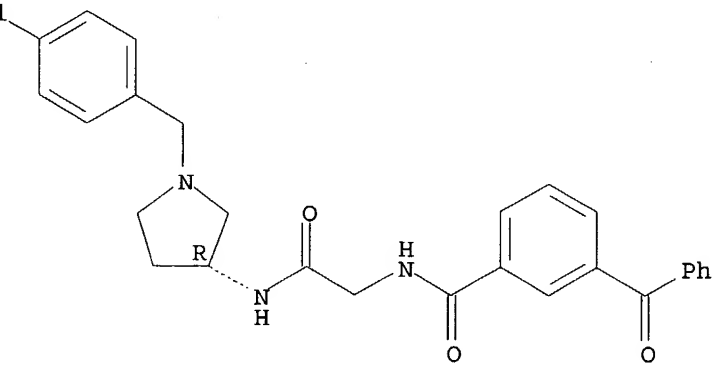
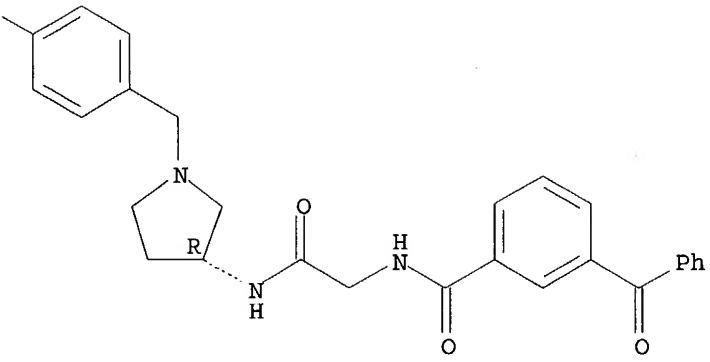


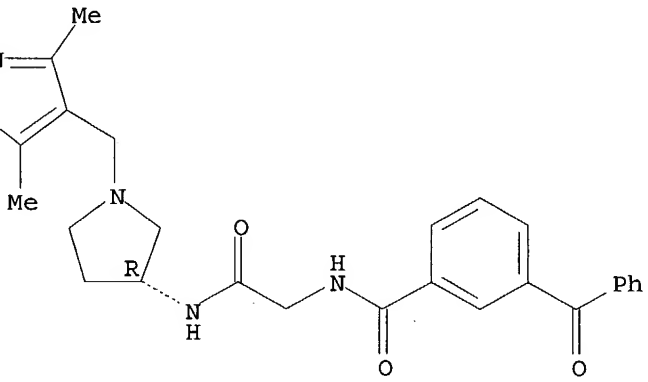
N 226241-35-6 CAPLUS
N Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-methylphenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

bsolute stereochemistry.



226241-39-0 CAPLUS
Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

solute stereochemistry.



226241-41-4 CAPLUS
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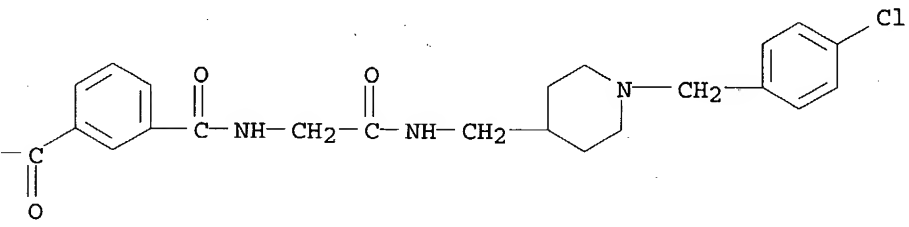
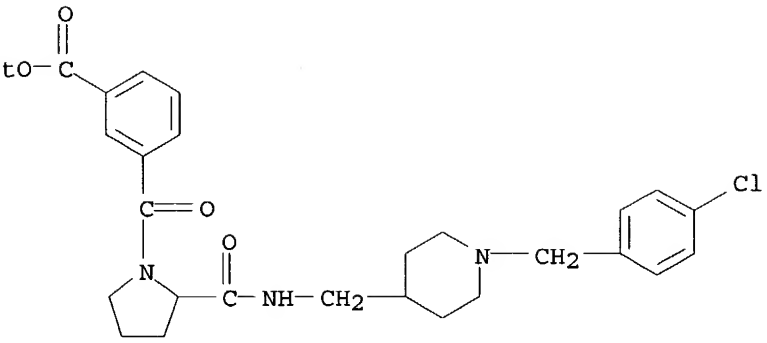
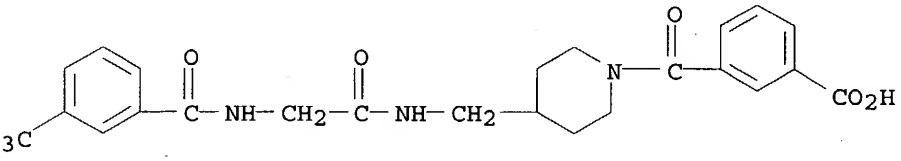


308360-90-9 CAPLUS
Benzoic acid, 3-[[2-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-1-pyrrolidinyl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



T **308363-03-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cyclic amine derivs. as remedies or preventives for diseases in association with chemokines or chemokine receptors)
N 308363-03-3 CAPLUS
N Benzoic acid, 3-[[4-[[[[[3-(trifluoromethyl)benzoyl]amino]acetyl]amino]methyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)



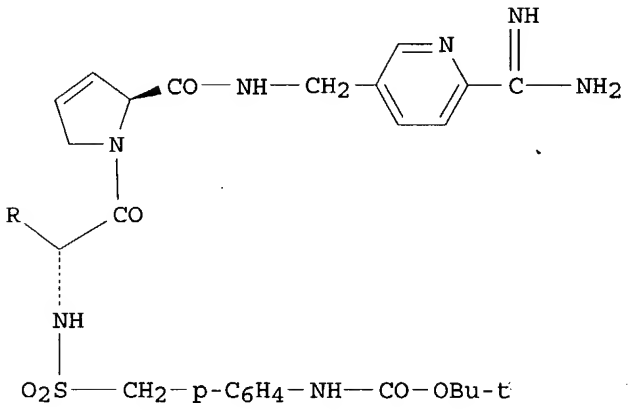
EFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

6 ANSWER 3 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
CCESSION NUMBER: 2000:742117 CAPLUS
OCUMENT NUMBER: 133:296665
ITLE: Preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases
NVENTOR(S): Hillen, Heinz; Schmidt, Martin; Mack, Helmut; Seitz, Werner; Haupt, Andreas; Zechel, Johann-Christian; Kling, Andreas
ATENT ASSIGNEE(S): BASF A.-G., Germany
OURCE: PCT Int. Appl., 212 pp.
CODEN: PIXXD2
OCUMENT TYPE: Patent
ANGUAGE: German
AMILY ACC. NUM. COUNT: 4
ATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000061608 | A2 | 20001019 | WO 2000-EP2710 | 20000328 <-- |
| WO 2000061608 | A3 | 20010111 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1169338 | A2 | 20020109 | EP 2000-920597 | 20000328 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200102913 | T2 | 20020121 | TR 2001-200102913 | 20000328 |
| BR 2000009678 | A | 20020122 | BR 2000-9678 | 20000328 |

| | | | | | |
|---|---|---|---|---|---|
| JP 2002542164 | T2 | 20021210 | JP 2000-611550 | | 20000328 |
| US 6683055 | B1 | 20040127 | US 2000-539811 | | 20000330 |
| ZA 2001007978 | A | 20030107 | ZA 2001-7978 | | 20010928 |
| BG 105978 | A | 20020731 | BG 2001-105978 | | 20011004 |
| NO 2001004876 | A | 20011204 | NO 2001-4876 | | 20011008 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19915930 | A | 19990409 |
| | | | WO 2000-EP2710 | W | 20000328 |

OTHER SOURCE(S): MARPAT 133:296665
GI



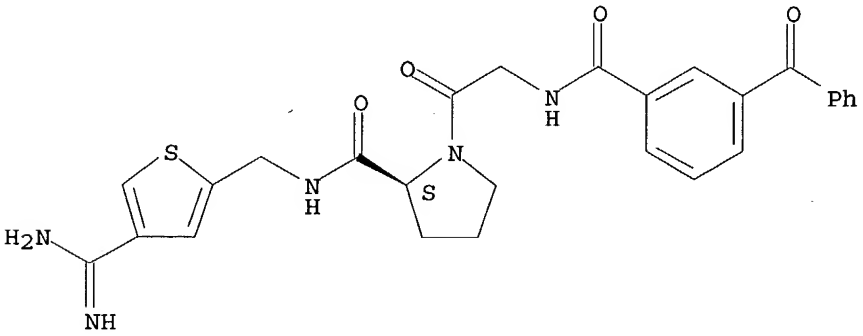
I

AB The invention relates to synthesis of title compds., e.g. [I; R = cyclohexyl(II) or R = cyclohexylmethyl(III)], for use as inhibitors of the complement proteases C1s and C1r in **treatment** of disease. Compound III was synthesized in seven steps, beginning with (D)-cyclohexylalanine Me ester hydrochloride and 4-nitrobenzylsulfonyl chloride, and including reaction with 3,4-dehydroprolyl-(3-(6-cyano)picolyl)-amide and conversion of the cyano group to the amidine. In in vivo expts. II had IC50's for C1s and C1r resp. of 0.6 and 0.9 μmol/l.

IT **301189-33-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amidine- or guanidine-containing peptidomimetics for use as inhibitors of complement proteases)

RN 301189-33-3 CAPLUS
CN L-Prolinamide, N-(3-benzoylbenzoyl)glycyl-N-[[4-(aminoiminomethyl)-2-thienyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 4 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:475535 CAPLUS
DOCUMENT NUMBER: 133:99557

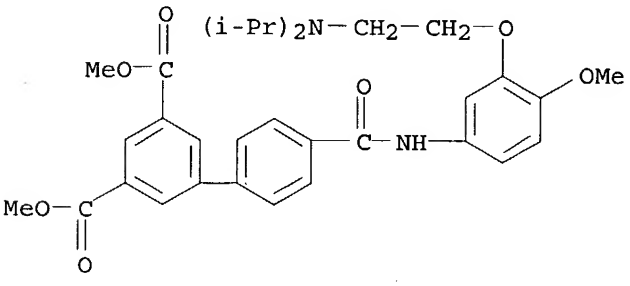
TITLE: Substituted benzanilides, their preparation, and their use as CCR5 receptor modulators
INVENTOR(S): Bondinell, William E.; Ku, Thomas W.; Wang, Ning
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000040239 | A1 | 20000713 | WO 1999-US30888 | 19991228 <-- |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 1140072 | A1 | 20011010 | EP 1999-967619 | 19991228 |
| EP 1140072 | B1 | 20040414 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2002534383 | T2 | 20021015 | JP 2000-591996 | 19991228 |
| AT 264100 | E | 20040415 | AT 1999-967619 | 19991228 |

PRIORITY APPLN. INFO.:
US 1998-114239P P 19981230
US 1999-128010P P 19990406
WO 1999-US30888 W 19991228

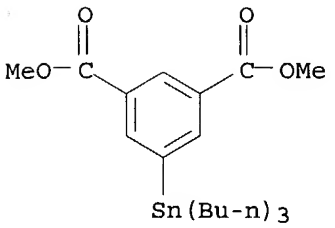
AB Substituted benzanilides are provided which are modulators, agonists or antagonists, of the CCR5 receptor. In addition, the invention relates to the **treatment** and prevention of disease states mediated by CCR5, including, but not limited to, asthma and atopic disorders (for example, atopic dermatitis and allergies), **rheumatoid arthritis**, sarcoidosis and other fibrotic diseases, atherosclerosis, psoriasis, autoimmune diseases such as multiple sclerosis, and inflammatory bowel disease, all in mammals, by the use of substituted benzanilides which are CCR5 receptor antagonists. Furthermore, since CD8+ T cells have been implicated in COPD, CCR5 may play a role in their recruitment and therefore antagonists to CCR5 could provide potential therapeutic in the **treatment** of COPD. Also, since CCR5 is a co-receptor for the entry of HIV into cells, selective receptor modulators may be useful in the **treatment** of HIV infection.

IT **282727-17-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(benzanilide derivative preparation and use as CCR5 receptor modulator)
RN 282727-17-7 CAPLUS
CN [1,1'-Biphenyl]-3,5-dicarboxylic acid, 4'-[[[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]amino]carbonyl]-, dimethyl ester (9CI) (CA INDEX NAME)




IT **210094-16-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; benzanilide derivative preparation and use as CCR5 receptor modulator)
RN 210094-16-9 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-(tributylstannyl)-, dimethyl ester (9CI)

(CA INDEX NAME)




REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:335229 CAPLUS
DOCUMENT NUMBER: 132:343358
TITLE: Cystine derivatives as therapeutic agents for matrix metalloprotease-related diseases
INVENTOR(S): Grams, Frank; Krell, Hans-Willi; Leinert, Herbert; Zimmermann, Gerd
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 2000027378 | A2 | 20000518 | WO 1999-EP8460 | | 19991105 <-- |
| WO 2000027378 | A3 | 20010920 | | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| BR 9915127 | A | 20010731 | BR 1999-15127 | | 19991105 |
| EP 1143960 | A2 | 20011017 | EP 1999-971709 | | 19991105 |
| EP 1143960 | A3 | 20011205 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| TR 200101222 | T2 | 20011221 | TR 2001-200101222 | | 19991105 |
| JP 2002529404 | T2 | 20020910 | JP 2000-580607 | | 19991105 |
| ZA 2001003605 | A | 20011211 | ZA 2001-3605 | | 20010504 |
| PRIORITY APPLN. INFO.: | | | EP 1998-121073 | A | 19981106 |
| | | | WO 1999-EP8460 | W | 19991105 |

OTHER SOURCE(S): MARPAT 132:343358

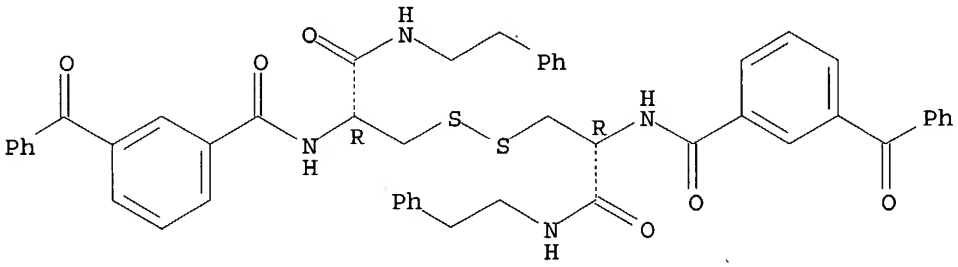
AB Pharmaceutical compns. are disclosed which contain nonpeptidic cystine derivs. R1ANHCH[CH2SSCH2CH(R3ANH)(C(O)NHR4)]C(O)NHR2 [R1, R3 = H, (non)aromatic carbocyclic or heterocyclic ring, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; R2, R4 = H, (un)branched (un)saturated C1-15 alkyl which can be interrupted by hetero atom and which can be substituted by (non)aromatic carbocyclic or heterocyclic ring; A = valency bond, CO, SO2, NHCO, NHCS or OC(O)], their pharmacol. acceptable salts and optically active forms thereof and pharmaceutically acceptable carriers, for the **treatment** of diseases selected from tumor growth and metastasis; inflammatory diseases, e.g. osteo- and **rheumatoid arthritis**; osteoporosis; multiple sclerosis; periodontitis; restenosis; diseases caused by bacteria, e.g. meningitis; sun-induced skin aging; and Alzheimer's disease. New compds. are also

disclosed.

IT **269067-09-6P 269067-10-9P 269067-11-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cystine derivative for **treatment** of matrix metalloprotease-related disease)

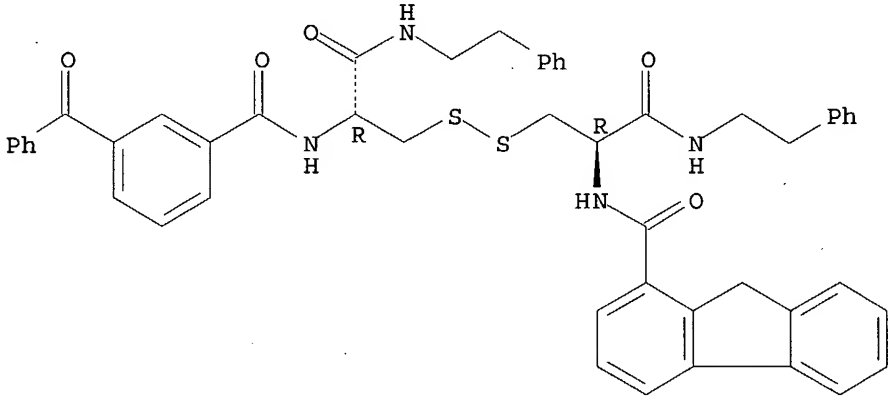
RN 269067-09-6 CAPLUS
CN Benzamide, N,N'-[dithiobis[(1R)-1-[[(2-phenylethyl)amino]carbonyl]-2,1-ethanediyl]]bis[3-benzoyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



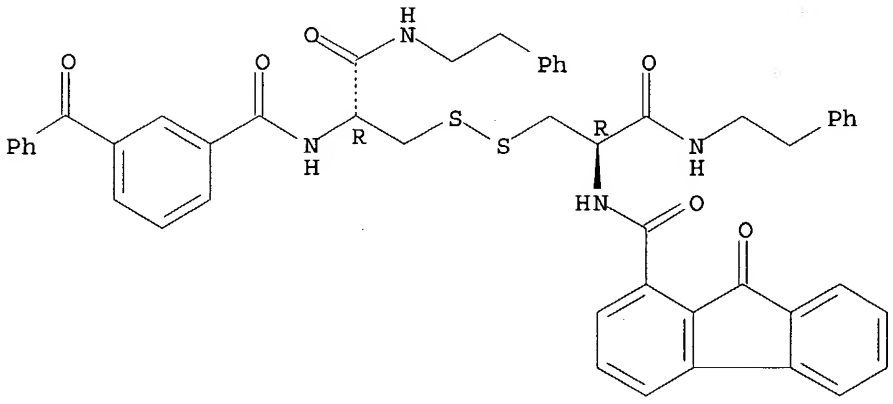
RN 269067-10-9 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 269067-11-0 CAPLUS
CN 9H-Fluorene-1-carboxamide, N-[(1R)-1-[[[(2R)-2-[(3-benzoylbenzoyl)amino]-3-oxo-3-[(2-phenylethyl)amino]propyl]dithio]methyl]-2-oxo-2-[(2-phenylethyl)amino]ethyl]-9-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L6 ANSWER 6 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:260225 CAPLUS
DOCUMENT NUMBER: 132:294010
TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors
INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000021920 | A1 | 20000420 | WO 1999-EP7620 | 19991012 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6331640 | B1 | 20011218 | US 1999-407534 | 19990929 |
| CA 2344058 | AA | 20000420 | CA 1999-2344058 | 19991012 <-- |
| BR 9914602 | A | 20010703 | BR 1999-14602 | 19991012 |
| EP 1121342 | A1 | 20010808 | EP 1999-953772 | 19991012 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| TR 200101038 | T2 | 20010921 | TR 2001-200101038 | 19991012 |
| JP 2002527416 | T2 | 20020827 | JP 2000-575829 | 19991012 |
| AU 766468 | B2 | 20031016 | AU 2000-10349 | 19991012 |
| ZA 2001002608 | A | 20020930 | ZA 2001-2608 | 20010329 |
| US 2002052512 | A1 | 20020502 | US 2001-879700 | 20010612 |
| US 2004006236 | A1 | 20040108 | US 2003-349289 | 20030122 |
| US 6803384 | B2 | 20041012 | | |

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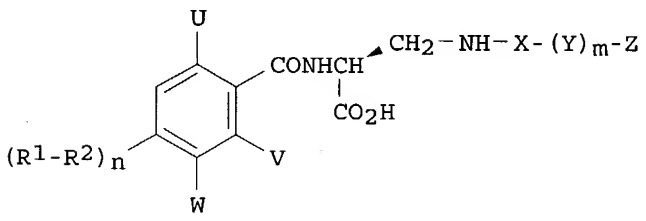
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1998-104120P | P | 19981013 |
| | US 1999-407534 | A3 | 19990929 |
| | WO 1999-EP7620 | W | 19991012 |
| | US 2001-879700 | B3 | 20010612 |

OTHER SOURCE(S): MARPAT 132:294010
GI




I

AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkylenethio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-

pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepared and are useful for **treating rheumatoid arthritis**, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of ischemia reperfusion injury, including acute myocardial infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepared by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-associated antigen-1)/ICAM-1 protein-protein assay.

IT **264273-81-6P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

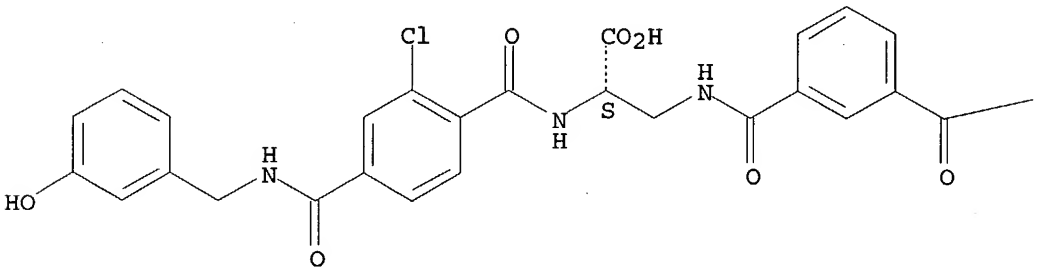
(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264273-81-6 CAPLUS

CN Benzoic acid, 3-[[[(2S)-2-carboxy-2-[[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]amino]ethyl]amino]carbonyl]-, 1-methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A




PAGE 1-B

—OMe

IT **264274-87-5P 264275-30-1P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

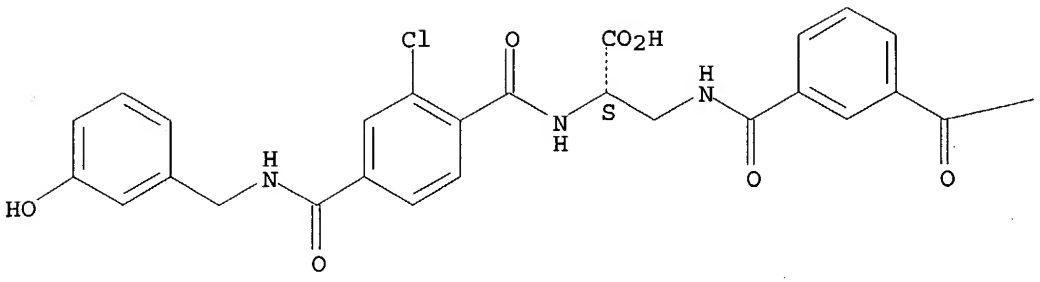
(preparation of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264274-87-5 CAPLUS

CN L-Alanine, 3-[[3-(aminocarbonyl)benzoyl]amino]-N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

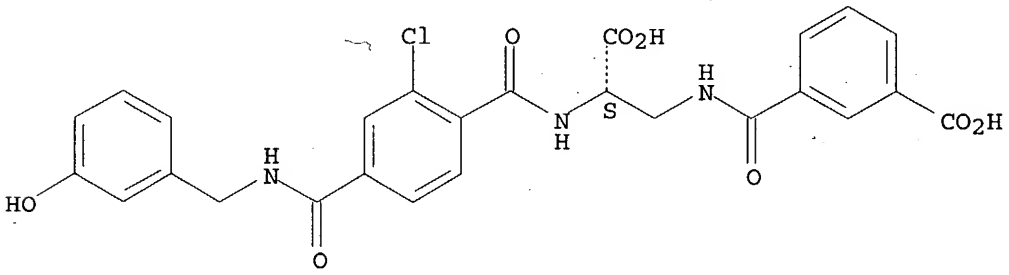


PAGE 1-B

—$NH_2$

RN 264275-30-1 CAPLUS
CN Benzoic acid, 3-[[[(2S)-2-carboxy-2-[[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]amino]ethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:98304 CAPLUS
DOCUMENT NUMBER: 132:151564
TITLE: Preparation of substituted anilides as modulators, agonists or antagonists of the CCR5 receptor
INVENTOR(S): Ku, Thomas W.; Bondinell, William E.; Neeb, Michael J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000006146 | A1 | 20000210 | WO 1999-US17121 | 19990728 <-- |
| W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2338764 | AA | 20000210 | CA 1999-2338764 | 19990728 <-- |

| | | | | | |
|---|---|---|---|---|---|
| AU 9952392 | A1 | 20000221 | AU 1999-52392 | | 19990728 <-- |
| BR 9912406 | A | 20010424 | BR 1999-12406 | | 19990728 |
| EP 1100485 | A1 | 20010523 | EP 1999-937589 | | 19990728 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | | |
| TR 200100267 | T2 | 20010921 | TR 2001-200100267 | | 19990728 |
| JP 2002521436 | T2 | 20020716 | JP 2000-562001 | | 19990728 |
| NO 2001000446 | A | 20010126 | NO 2001-446 | | 20010126 |
| PRIORITY APPLN. INFO.: | | | US 1998-94406P | P | 19980728 |
| | | | US 1999-134157P | P | 19990514 |
| | | | WO 1999-US17121 | W | 19990728 |

OTHER SOURCE(S): MARPAT 132:151564

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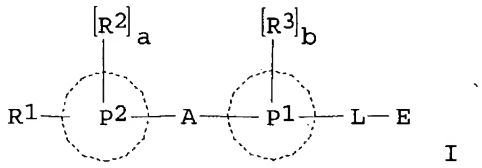


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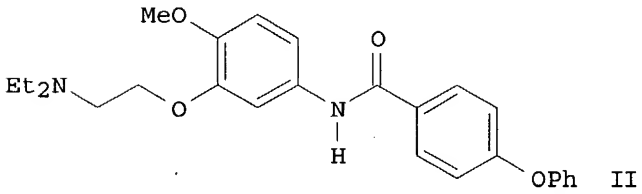



II

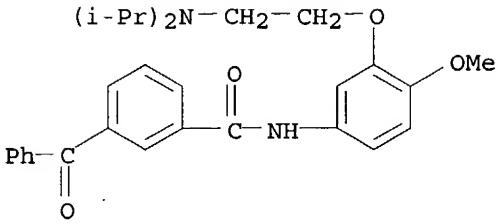
AB The title compds. [I; the basic N in moiety E may be optionally quaternized with alkyl or is optionally present as the N-oxide; P1, P2 = Ph, fused bicyclic aryl, monocyclic heterocyclyl, etc.; A = CO, O, SOc, etc.; L = CH2NH, NHCH2, etc.; R1, R2 = H, alkyl, alkenyl, etc.; R3 = H, alkyl, cycloalkyl, etc.; a, b = 1-3; c = 0-2] which are modulators, agonists or antagonists of the CCR5 receptor, and therefore useful in **treating** COPD, asthma and atopic disorders, **rheumatoid arthritis**, atherosclerosis, sarcoidosis and other fibrotic disease, psoriasis, autoimmune diseases such as multiple sclerosis, inflammatory bowel disease, and HIV, were prepared E.g., a synthesis of benzamide II starting with (4-formyl-3,5-dimethoxyphenoxy)-Merrifield resin and 3-[2-(diethylamino)ethoxy]-4-methoxyaniline, was given. Compds. I show CCR5 receptor modulator activity having IC50 values of 0.0001 to 100 μM.

IT **257616-21-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted anilides as modulators, agonists or antagonists of the CCR5 receptor)

RN 257616-21-0 CAPLUS

CN Benzamide, 3-benzoyl-N-[3-[2-[bis(1-methylethyl)amino]ethoxy]-4-methoxyphenyl]- (9CI) (CA INDEX NAME)

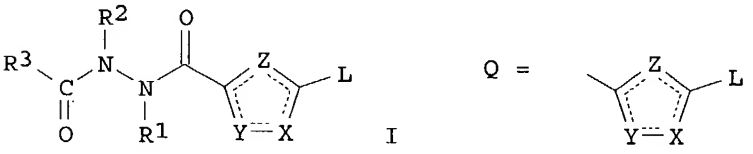


REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:819241 CAPLUS
DOCUMENT NUMBER: 132:64530
TITLE: Preparation of diacyl hydrazine compds. as protease inhibitors
INVENTOR(S): Halbert, Stacie Marie; Michaud, Evelyne; Thompson, Scott Kevin; Veber, Daniel Frank
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 167 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9966925 | A1 | 19991229 | WO 1999-US14561 | 19990624 <-- |
| W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2335876 | AA | 19991229 | CA 1999-2335876 | 19990624 <-- |
| AU 9947237 | A1 | 20000110 | AU 1999-47237 | 19990624 <-- |
| EP 1093367 | A1 | 20010425 | EP 1999-930779 | 19990624 |
| R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| JP 2002518444 | T2 | 20020625 | JP 2000-555611 | 19990624 |
| PRIORITY APPLN. INFO.: | | | US 1998-90493P | P 19980624 |
| | | | WO 1999-US14561 | W 19990624 |

OTHER SOURCE(S): MARPAT 132:64530
GI



AB The present invention provides compds. I [L = C2-6 alkyl, Ar- or Het-C0-6 alkyl, CHR4NR5R6, CHR4Ar, CHR4OAr, NR4R7; X, Y, Z = N, O, S, CR10; R1, R2, R5, R10 = H, C1-6 alkyl, C2-6 alkenyl, Ar- or Het-C0-6 alkyl; R3 = C3-6 alkyl, Ar, Het, heterocycle Q, etc.; R4 = H, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, Ar- or Het-C0-6 alkyl, etc.; R6 = R14 or an acyl group such as R14CO, R14C(S), R14OCO (R14 = C1-6 alkyl, C2-6 alkenyl, Ar- or Het C0-6 alkyl); R7 = C1-6 alkyl, C1-6 alkenyl, C3-6 cycloalkyl-, Ar-, or Het-C0-6 alkyl], which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis, gingival disease, and arthritis. Thus, N-[2-[N-cyclopropyl-N-(cyclopropylmethyl)amino]thiazol-4-ylcarbonyl]-N'-[N-(6-methyl-3-

pyridinylmethoxycarbonyl)-L-β-tert-butylalanyl]hydrazide was prepared via sequential reactions of Et 6-nicotinate, L-β-tert-butylalanine, cyclopropylamine, cyclopropylcarboxaldehyde, benzoyl isothiocyanate, and Et bromopyruvate.

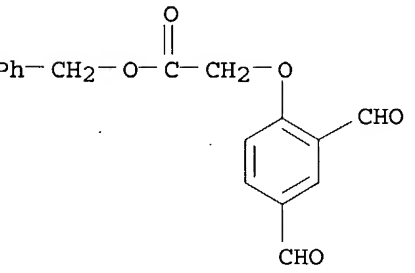
IT **250726-45-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of diacyl hydrazine compds. as protease inhibitors)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)




REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:753240 CAPLUS

DOCUMENT NUMBER: 132:11677

TITLE: Isolation of physiologically active VD1207 substances having a neovascularization inhibitory effect from Streptomyces strain

INVENTOR(S): Wakabayashi, Toshiaki; Kawase, Rena; Naruse, Nobuaki; Fujita, Masanori; Sameshima, Tomohiro; Watanabe, Yoshio; Dobashi, Kazuyuki; Funahashi, Yasuhiro; Senba, Taro

PATENT ASSIGNEE(S): Mercian Corporation, Japan; Eisai Co., Ltd.

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

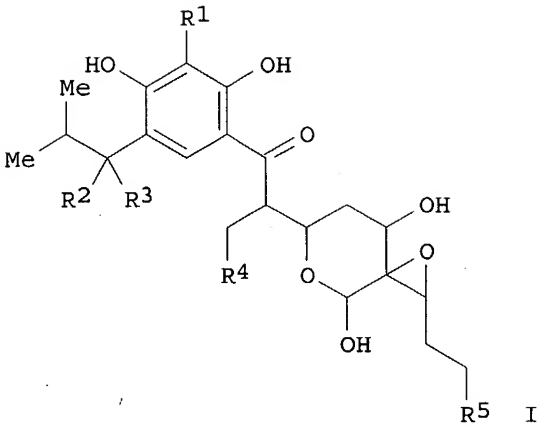
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9960000 | A1 | 19991125 | WO 1999-JP2288 | 19990428 <-- |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9935386 | A1 | 19991206 | AU 1999-35386 | 19990428 <-- |
| EP 1081151 | A1 | 20010307 | EP 1999-917219 | 19990428 |
| R: DE, FR, GB | | | | |
| US 6645996 | B1 | 20031111 | US 2000-700680 | 20001117 |
| PRIORITY APPLN. INFO.: | | | JP 1998-135205 A | 19980518 |
| | | | WO 1999-JP2288 W | 19990428 |

OTHER SOURCE(S): MARPAT 132:11677

GI



AB The title 6-(5-isobutyl-2,4-dihydroxyphenacyl)-4,8-dihydroxy-1,5-dioxaspiro[2.5]octane compds. represented by general formula (I; R1 represents hydrogen, aldehyde or lower acyl; R2 and R3 may be the same or different and each represents hydrogen or lower alkoxy, or R2 and R3 may represent together oxygen; R4 represents lower alkyl; and R5 represents hydrogen or lower alkyl, provided that the case where R1 is aldehyde, R2 and R3 are different from each other and represent hydrogen or methoxy, R4 is Et and R5 is hydrogen is excluded) or salts thereof are isolated from a liquid culture medium of a strain belonging to the genus Streptomyces and the structures are analyzed. Also claimed are drugs based on inhibiting the expression of adhesion mols. VCAM-1 or/and E-selectin containing I as the active ingredients. These compds. are useful for the **treatment** and prevention of **rheumatoid arthritis**, solid tumor, atherosclerosis, diabetic retinopathy, vascular tumors, and psoriasis. Thus, Streptomyces sp. VD1207 was aerobically cultured in a medium containing glycerol 2, glucose 2, soybean meal 2, yeast extract 0.5, NaCl 0.25, CaCO3 0.32, CuSO4.5H2O 0.0005, MnCl2.4H2O 0.0005, and ZnSO4.7H2O 0.0005% at 28° for 64 h (2 culture tanks each containing 100 L medium) and centrifuged to remove the bacteria followed by chromatog. separation using a Diaion HP-20 column, a YMC-GEL ODS-AM 120-S50 column and silica gel chromatog., HPLC separation, or thin layer chromatog. to give VD1207U1 [(+)-I; R1 = R5 = H, R2R3 = O, R4 = Et], VD1207U2 [(-)-I; R1 = R5 = H, R2R3 = O, R4 = Et], VD1207A1 [(+)-I; R1 = R5 = H, R2R3 = O, R4 = i-Pr], VD1207A2 [(-)-I; R1 = R5 = H, R2R3 = O, R4 = i-Pr], VD1207B [(-)-I; R1 = CHO; R2, R3 = OMe, H; R4 = Et, R5 = H], VD1207C [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = Et, R5 = H], VD1207D [(-)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = Et], VD1207E [(-)-I; R1 = CHO; R2, R3 = OMe, H; R4 = i-Pr, R5 = H], VD1207F [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = i-Pr, R5 = H], VD1207F' [(+)-I; R1 = CHO; R2, R3 = OMe, H; R4 = n-Pr, R5 = H], VD1207G' [(-)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = n-Pr], VD1207G1 [(-)-I; R1 = CHO, R2 = R3 = H, R4 = Et, R5 = Me], VD1207G2 [(+)-I; R1 = CHO, R2 = R3 = R5 = H, R4 = i-Pr], and VD1207H [(-)-I; R1 = COMe, R2 = R3 = R5 = H, R4 = Et]. In a neovascularization inhibitory assay, VD1207 A2, B, C, D, E, F, F', G1, G2, G', and H in vitro showed IC50 of 1, 0.053, 0.050, 0.019, 0.047, 0.067, 0.10, 0.070, 0.034, 0.11, and 0.38 μg/mL, resp., for inhibiting the formation of capillary vessel in rat aorta cultured in collagen.

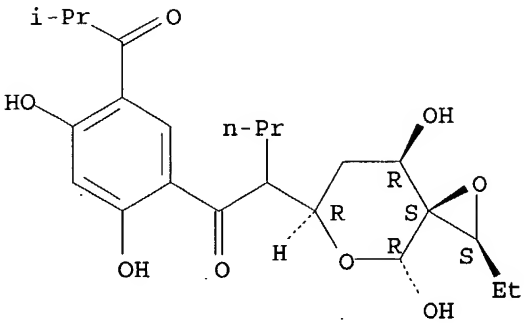
IT **251449-85-1P**, VD 1207U1 **251449-86-2P**, VD 1207U2
**251449-87-3P**, VD 1207A1 **251449-88-4P**, VD 1207A2
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(isolation of physiol. active VD1207 substances having neovascularization inhibitory effect from Streptomyces sp. VD1207)

RN 251449-85-1 CAPLUS

CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]- (9CI) (CA INDEX NAME)

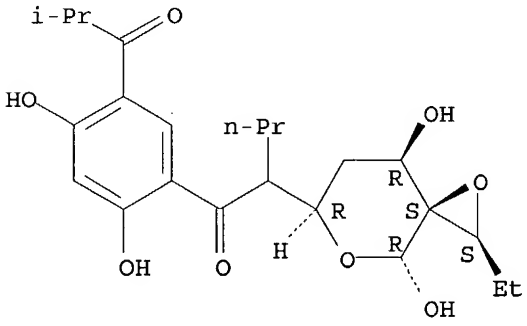
Absolute stereochemistry. Rotation (+).

Currently available stereo shown.



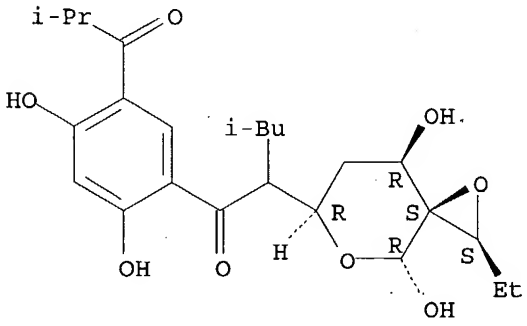

RN 251449-86-2 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Currently available stereo shown.



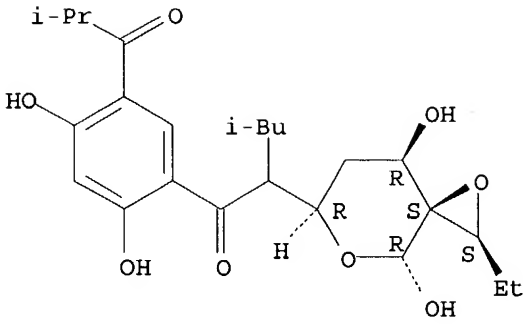

RN 251449-87-3 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Currently available stereo shown.




RN 251449-88-4 CAPLUS
CN 1-Pentanone, 1-[2,4-dihydroxy-5-(2-methyl-1-oxopropyl)phenyl]-2-[(2S,3S,4R,8R)-2-ethyl-4,8-dihydroxy-1,5-dioxaspiro[2.5]oct-6-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Currently available stereo shown.




REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753058 CAPLUS
DOCUMENT NUMBER: 132:426
TITLE: Diacyl carbohydrazide compds. as protease inhibitors for **treating** diseases of excessive bone loss or cartilage or matrix degradation
INVENTOR(S): Halbert, Stacie Marie; Thompson, Scott Kevin; Veber, Daniel Frank
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9959570 | A1 | 19991125 | WO 1998-US17275 | 19980820 <-- |
| W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2332492 | AA | 19991125 | CA 1998-2332492 | 19980820 <-- |
| AU 9891102 | A1 | 19991206 | AU 1998-91102 | 19980820 <-- |
| EP 1079821 | A1 | 20010307 | EP 1998-943273 | 19980820 |
| R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | |
| JP 2002515428 | T2 | 20020528 | JP 2000-549235 | 19980820 |

PRIORITY APPLN. INFO.: US 1998-86553P P 19980521
WO 1998-US17275 W 19980820

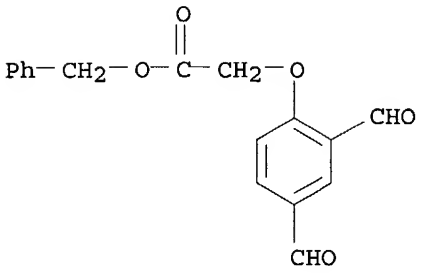
OTHER SOURCE(S): MARPAT 132:426

AB The present invention provides diacyl carbohydrazide compds., and pharmaceutically acceptable salts, hydrates and solvates thereof, which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., novel intermediates of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, **osteoarthritis** and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention.

IT **250726-45-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(diacyl carbohydrazide compds. as protease inhibitors for **treating** diseases of excessive bone loss or cartilage or matrix degradation)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)

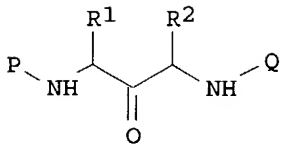


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 11 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:753019 CAPLUS
DOCUMENT NUMBER: 132:12506
TITLE: Preparation of peptides for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors
INVENTOR(S): Bondinell, William Edward; Desjarlais, Renee Louise; Veber, Daniel Frank; Yamashita, Dennis Shinji
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| WO 9959526 | A2 | 19991125 | WO 1999-US11266 | | 19990520 <-- |
| WO 9959526 | A3 | 20000120 | | | |
| W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | | |
| CA 2332531 | AA | 19991125 | CA 1999-2332531 | | 19990520 <-- |
| EP 1067894 | A2 | 20010117 | EP 1999-924421 | | 19990520 |
| R: BE, CH, DE, ES, FR, GB, IT, LI, NL | | | | | |
| JP 2002515411 | T2 | 20020528 | JP 2000-549192 | | 19990520 |
| US 6518267 | B1 | 20030211 | US 2000-700828 | | 20001121 |
| PRIORITY APPLN. INFO.: | | | US 1998-86557P | P | 19980521 |
| | | | WO 1999-US11266 | W | 19990520 |

OTHER SOURCE(S): MARPAT 132:12506
GI



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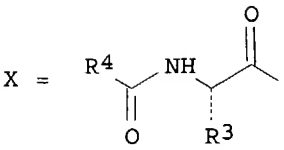
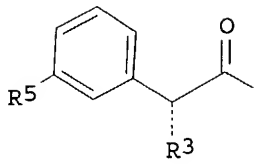
X = 

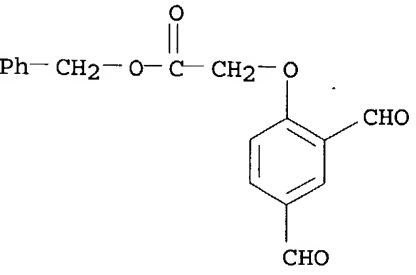
Y = 

AB The present invention provides peptides bis-aminomethyl carbonyl protease inhibitors I (R1, R2 = alkyl; P = X, Y; R3 selected from the group consisting of: CH2CH(CH3)2, CH2CH2CH3, CH2CH=CH2, or CH2Ph; R4 is selected from the group consisting of alkyl; N-piperazine; N-tetrahydroisoquinoline; substituted alkyl, Ph, benzofuran, benzothiazole; quinoline; naphthyl; and benzoxazole; R5 = Ph and Ph substituted with alkyl, N-piperidine, benzofuran; pyridine; Q = arylacyl) and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for **treating** diseases of excessive bone loss or cartilage or matrix degradation, including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, **osteoarthritis** and **rheumatoid arthritis**; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degradation by administering to a patient in need thereof a compound of the present invention. Thus, (S)-3N-(N-(thianaphthenyl-2-carbonyl)-leucinyl)-amino-1N-(3-{2-(1-oxo)-pyridyl}phenylacetyl)-amino-butan-2-one was prepared for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitor. Determination of cathepsin K proteolytic catalytic activity of these compds. are reported.

IT **250726-45-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for **treating** diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors)

RN 250726-45-5 CAPLUS

CN Acetic acid, (2,4-diformylphenoxy)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 12 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:566043 CAPLUS

DOCUMENT NUMBER: 131:199620

TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors

INVENTOR(S): Seehra, Jasbir S.; Xiang, Yibin; Bemis, Jean; McKew, John; Kaila, Neelu; Chen, Lihren

PATENT ASSIGNEE(S): Genetics Institute, Inc., USA

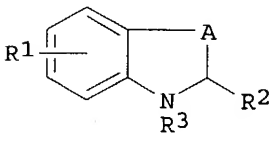
SOURCE: PCT Int. Appl., 225 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9943672 | A1 | 19990902 | WO 1999-US3388 | 19990217 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2322163 | AA | 19990902 | CA 1999-2322163 | 19990217 <-- |
| AU 9932970 | A1 | 19990915 | AU 1999-32970 | 19990217 <-- |
| BR 9909242 | A | 20001114 | BR 1999-9242 | 19990217 <-- |
| TR 200002445 | T2 | 20001221 | TR 2000-200002445 | 19990217 <-- |
| EP 1062216 | A1 | 20001227 | EP 1999-936073 | 19990217 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| JP 2002504551 | T2 | 20020212 | JP 2000-533428 | 19990217 |
| EE 200000522 | A | 20020215 | EE 2000-522 | 19990217 |
| HR 2000000513 | A1 | 20011231 | HR 2000-513 | 20000731 |
| NO 2000004217 | A | 20001023 | NO 2000-4217 | 20000823 <-- |
| BG 104781 | A | 20011031 | BG 2000-104781 | 20000919 |

PRIORITY APPLN. INFO.:
US 1998-30102 A 19980225
WO 1999-IS3388 W 19990217
WO 1999-US3388 W 19990217

OTHER SOURCE(S): MARPAT 131:199620
GI



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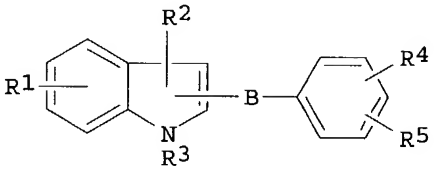

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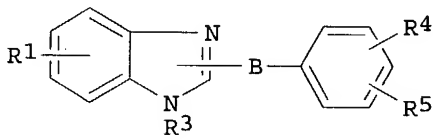

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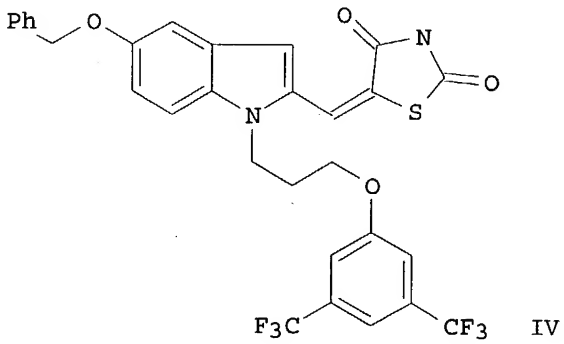


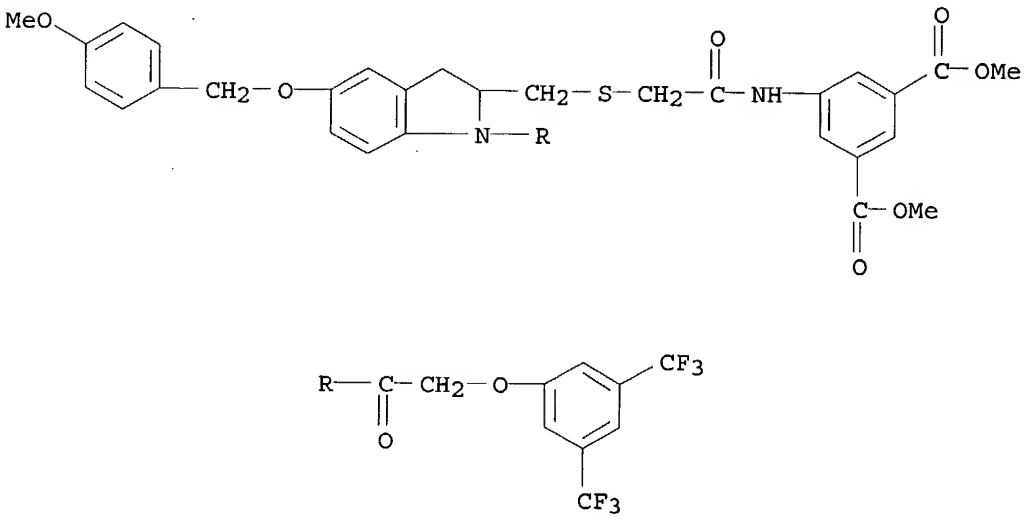
IV

AB Indole derivs. (I), (II), and (III) [where A = CH2 or CH2CH2; B = (CH2)n, (CH2O)n, (CH2S)n, (OCH2)n, (SCH2)n, (CH=CH)n, (C.tplbond.C)n, CON(R6), N(R6)CO, O, S, or N(R6); R1 and R5 = independently H, OH, halogen, CN, NO2, C1-5 alkyl, alkenyl, alkynyl, or (un)substituted aryl, etc.; R2 and

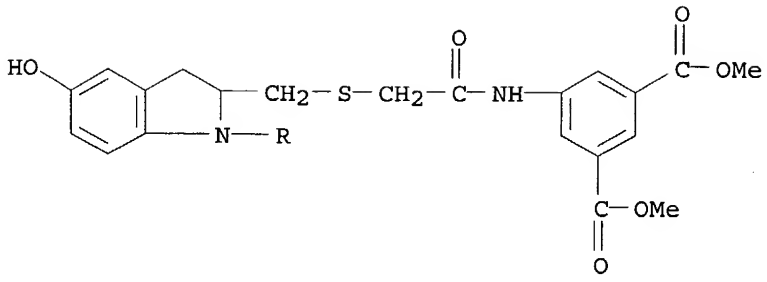
R3 = independently H, CO2H, COR5, CONR5R6, (CH2)nW(CH2)mZR5, (CH2)nWR5, ZR5, C1-10 alkyl, alkenyl, or substituted aryl; R4 = H, OH, OR6, SR6, CN, COR6, NHR6, CO2H, COR6R7, NO2, (un)substituted sulfamidocarbonyl, C1-5 alkyl, alkenyl, or substituted aryl; R6, R7 = H, C1-5 alkyl, alkenyl, alkynyl, or (un)substituted aryl; W = O, S, CH2, CH=CH, C.tplbond.C, or N(R6); X = O, S, N(R6); Z = CH2, O, S, N(R6), CO, CON(R6), N(R6)CO; m and n = independently 0-4] and pharmaceutically acceptable salts thereof, were prepared Thus, 2,4-thiazolidinedione and K2CO3 followed by NaOH were added to 5-(benzyloxyl)-1-(4-{[3,5-bis(trifluoromethyl)phenoxy]methyl}benzyl)-1H-indole-2-carboxaldehyde in EtOH to form the 2,4-thiazolidinedion-4-ylidene derivative The ylidene was dissolved in a solution of DMF and NaH, reacted with an alkyl ester of 4-(bromomethyl)benzoic acid, and deesterified with HF to yield the acid, (E)-(IV). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired. Eighty-seven compds. of the invention were tested for phospholipase enzyme inhibiting activity in the LysoPC and/or Coumarine assay. IC50 values ranged from 0.081 μM to >50 μM for the LysoPC assay and from 2.5 μM to >64 μM for the Coumarine assay. Selected compds. were tested for in vivo activity in the carrageenan-induced rat paw edema test, and showed 4.2% to 34.2% inhibition. Forty-eight compds. of the invention were tested for cPLA2 enzyme activity, and exhibited 25% to 95% inhibition at concns. of 3 μM to 100 μM.

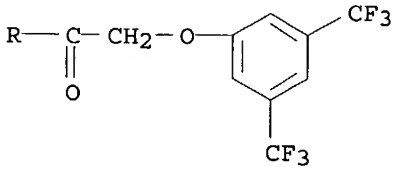
IT **204017-40-3P 204017-41-4P 204017-42-5P**
**204017-63-0P 204017-64-1P 204017-65-2P**
**204017-75-4P 204017-76-5P 204017-77-6P**
**241490-04-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 204017-40-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

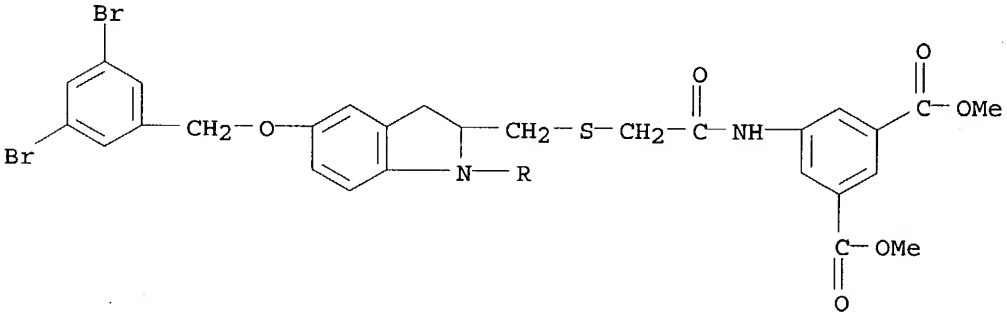


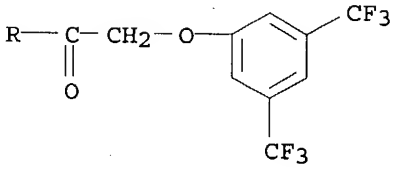

RN 204017-41-4 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-hydroxy-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



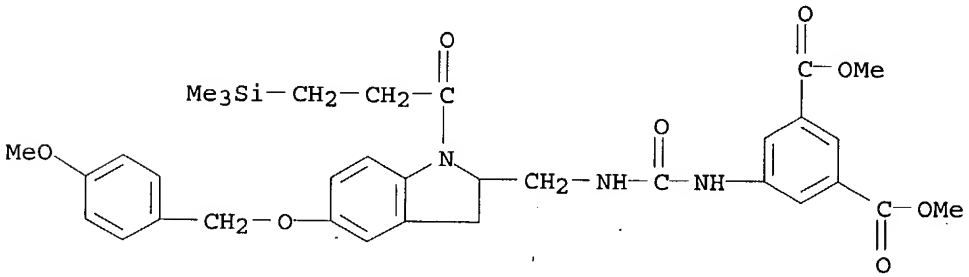


RN 204017-42-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-5-[(3,5-dibromophenyl)methoxy]-2,3-dihydro-1H-indol-2-yl]methyl]thio]acetyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



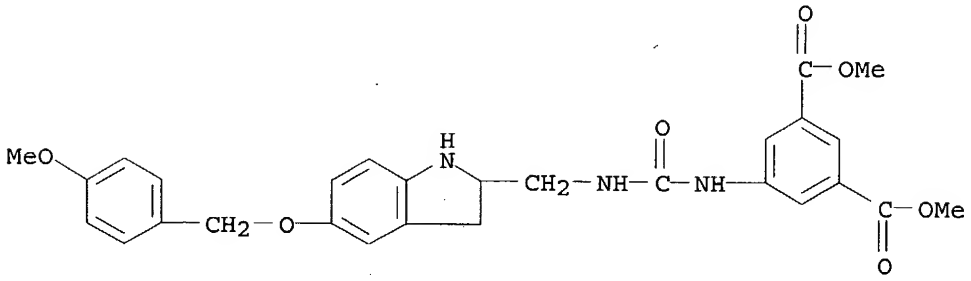


RN 204017-63-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1-[1-oxo-3-(trimethylsilyl)propyl]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

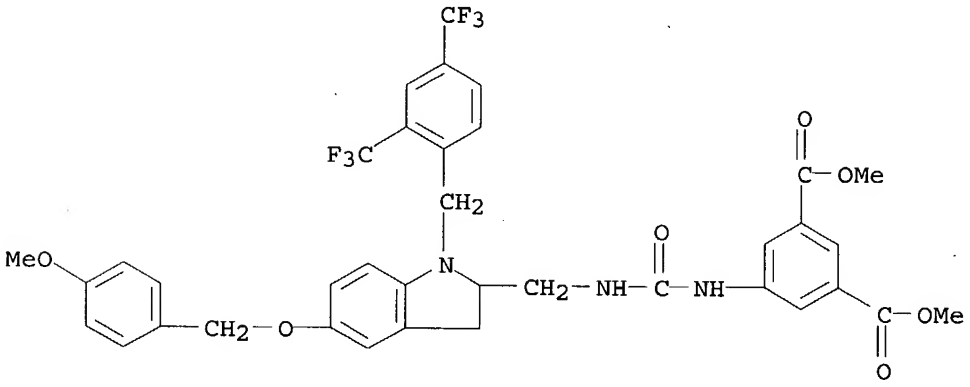


RN 204017-64-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[2,3-dihydro-5-[(4-

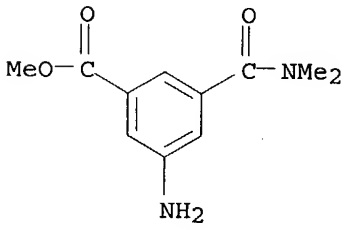
methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 204017-65-2 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2,3-dihydro-5-[(4-methoxyphenyl)methoxy]-1H-indol-2-yl]methyl]amino]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 204017-75-4 CAPLUS
CN Benzoic acid, 3-amino-5-[(dimethylamino)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



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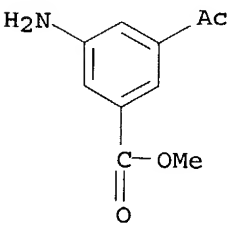
CN Benzoic acid, 3-acetyl-5-amino-, methyl ester (9CI) (CA INDEX NAME)



RN 204017-77-6 CAPLUS
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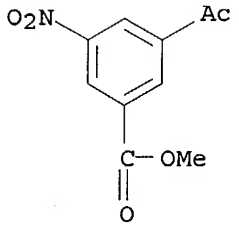

RN 241490-04-0 CAPLUS
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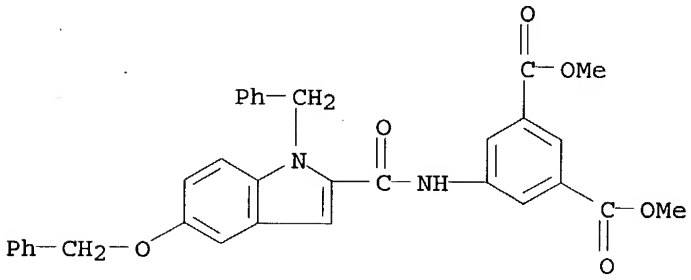

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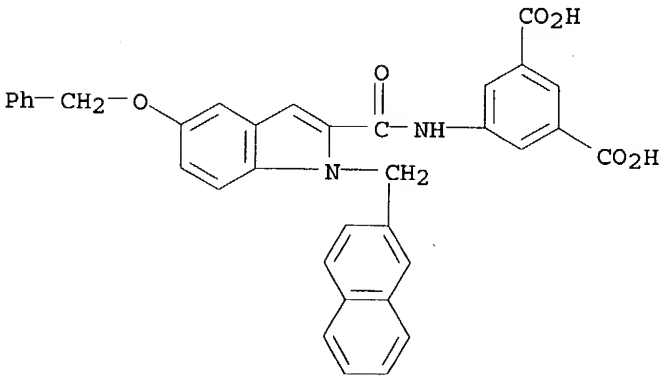
**204016-45-5P 204016-64-8P 204016-65-9P**
**204016-66-0P 204016-69-3P 204017-09-4P**
**204017-12-9P 204017-13-0P 241489-80-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)
RN 204016-33-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



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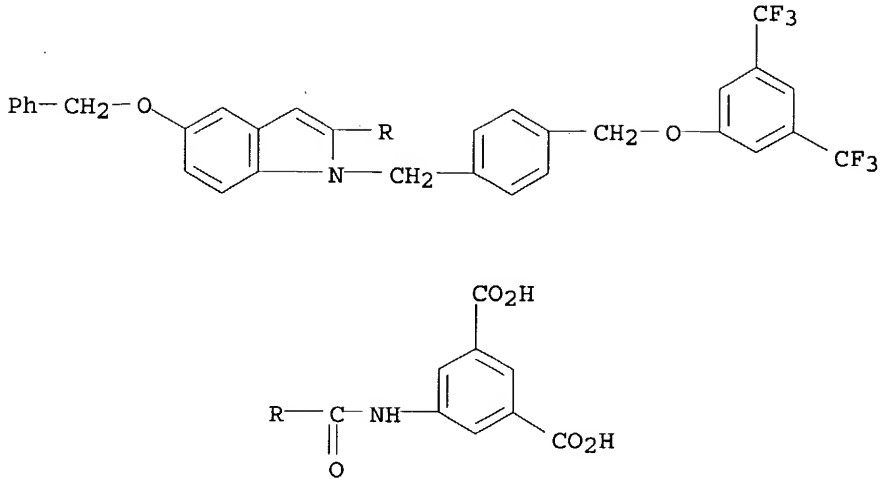
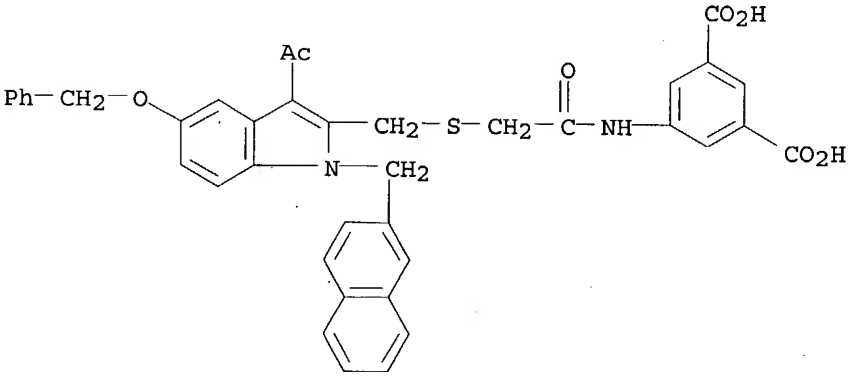
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[4-[[3,5-bis(trifluoromethyl)phenoxy]methyl]phenyl]methyl]-5-(phenylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 204016-42-2 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[3-acetyl-1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)



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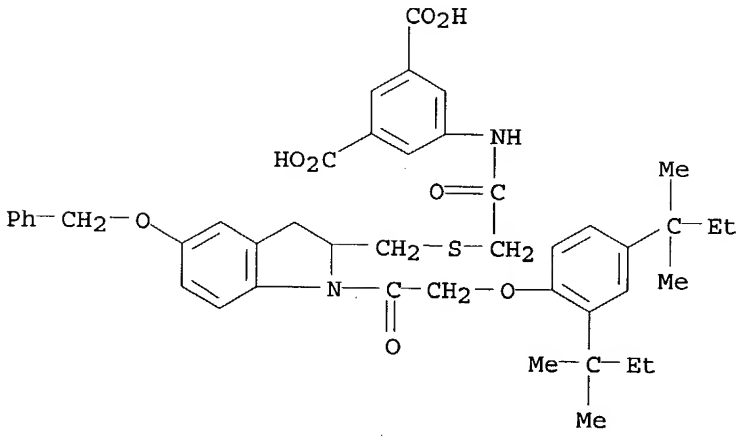
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[2,4-bis(1,1-dimethylpropyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)



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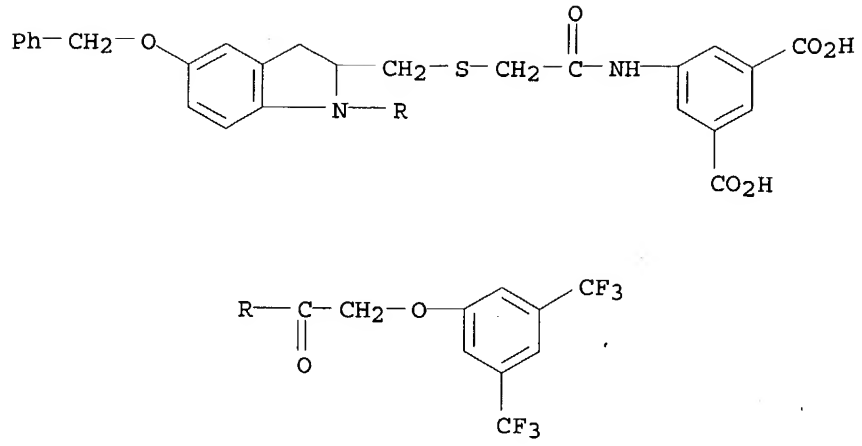
CN 1,3-Benzenedicarboxylic acid, 5-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]- (9CI) (CA INDEX NAME)





RN 204016-65-9 CAPLUS
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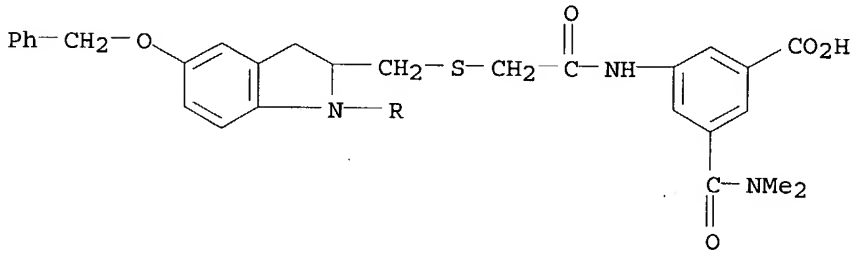

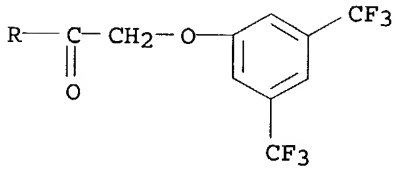

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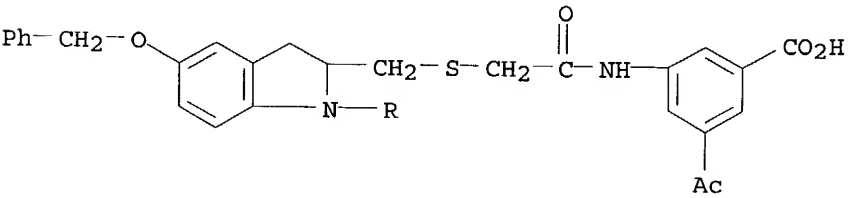
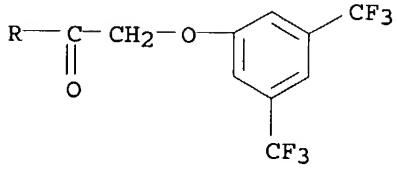
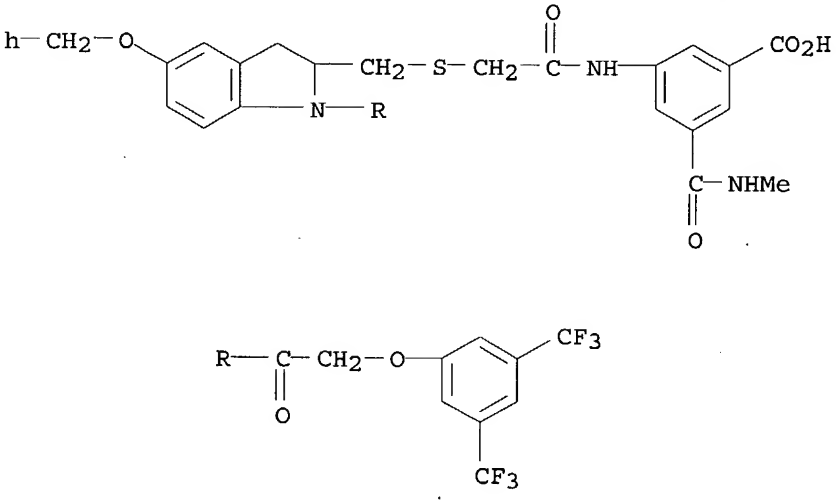


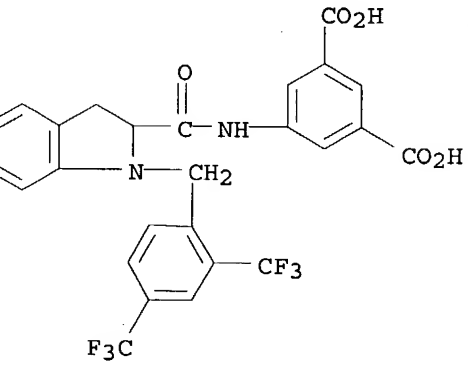


LN 204016-69-3 CAPLUS
'N Benzoic acid, 3-[[[[[1-[[3,5-bis(trifluoromethyl)phenoxy]acetyl]-2,3-dihydro-5-(phenylmethoxy)-1H-indol-2-yl]methyl]thio]acetyl]amino]-5-[(methylamino)carbonyl]- (9CI) (CA INDEX NAME)





N 204017-09-4 CAPLUS
N 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2,3-dihydro-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



N 204017-12-9 CAPLUS
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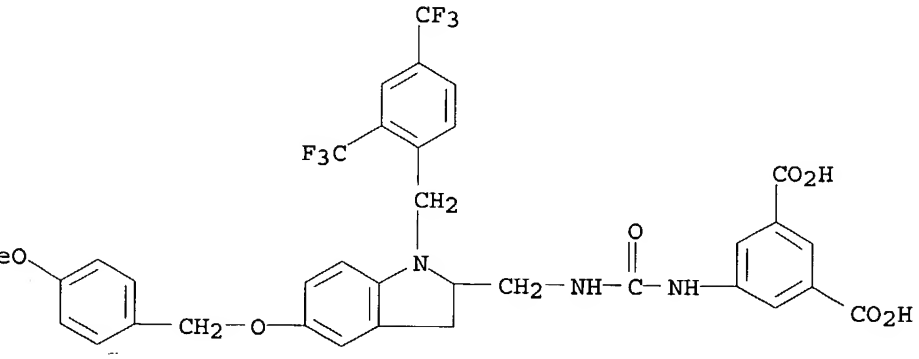

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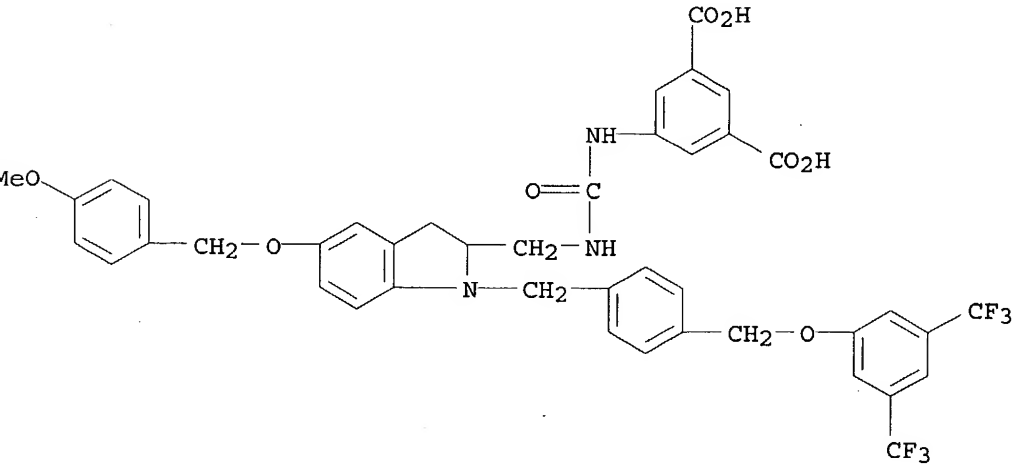

RN 241489-80-5 CAPLUS
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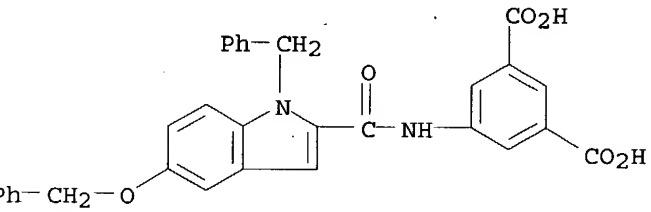

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 13 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:566026 CAPLUS
DOCUMENT NUMBER: 131:199619
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Mckew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin; Chen, Lihren; Knopf, John L.
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9943654 | A2 | 19990902 | WO 1999-US3898 | 19990224 <-- |
| WO 9943654 | A3 | 19991028 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| AU 765427 | B2 | 20030918 | | | |
| BR 9908275 | A | 20001024 | BR 1999-8275 | 19990224 | <-- |
| TR 200002447 | T2 | 20001121 | TR 2000-200002447 | 19990224 | <-- |
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| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | | |
| JP 2002504541 | T2 | 20020212 | JP 2000-533412 | 19990224 | |
| EE 200000488 | A | 20020215 | EE 2000-488 | 19990224 | |
| NZ 506329 | A | 20040130 | NZ 1999-506329 | 19990224 | |
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| HR 2000000551 | A1 | 20010430 | HR 2000-551 | 20000824 | |
| BG 104779 | A | 20011031 | BG 2000-104779 | 20000919 | |

PRIORITY APPLN. INFO.: US 1998-30592 A 19980225
WO 1999-US3898 W 19990224

OTHER SOURCE(S): MARPAT 131:199619

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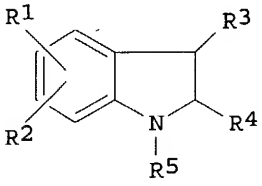


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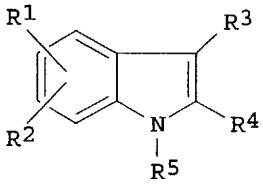


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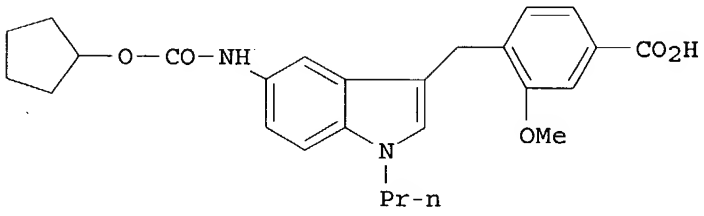



III

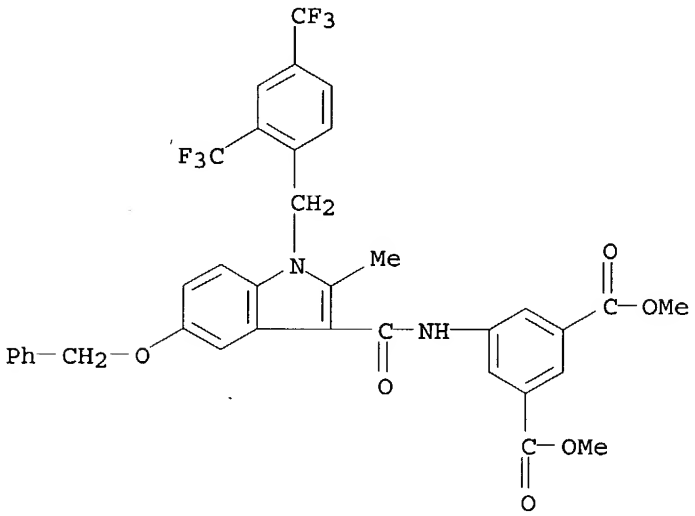
AB Indole derivs. (I) and (II) [where R1 = H, halogen, CF3, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, NH2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.; R4 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, CHO, halogen, etc.; R5 = C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.] and pharmaceutically acceptable salts thereof, were prepared by several methods. Thus, 5-nitroindole was C3-alkylated with Me 4-(bromomethyl)-3-methoxybenzoate in dioxane, N-alkylated with 1-iodopropane in a solution of THF and NaH, and converted to the amine by hydrogenation over Pt/C. The amine was converted to the carbamate by addition of cyclopentyl chloroformate in CH2Cl2 and 4-methylmorpholine and the resultant ester hydrolyzed to yield 4-[(5-{[(cyclopentyloxy)carbonyl]amino}-1-propyl-1H-indol-3-yl)methyl]-3-methoxybenzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired. Over one hundred compds. of the invention were tested for cPLA2 inhibiting activity in the Coumarine assay and rat carrageenan-induced footpad edema test. Compds. exhibited 7% to 98% inhibition at concns. of 0.125 μM to 400 μM in the Coumarine assay and -7.16% to 34.52% inhibition at concns. of 2 μM to 20 μM in the footpad edema test.

IT **241498-37-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

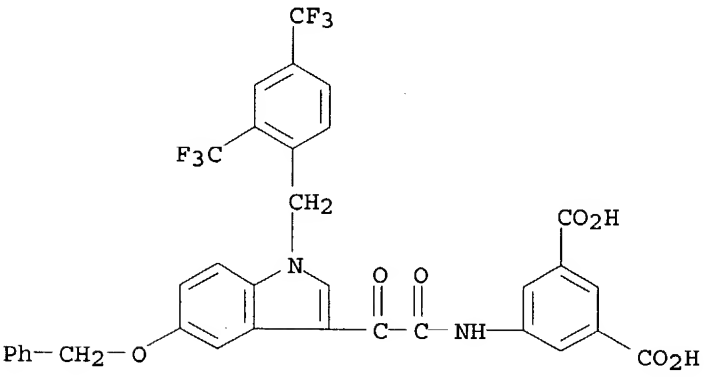
(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241498-37-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

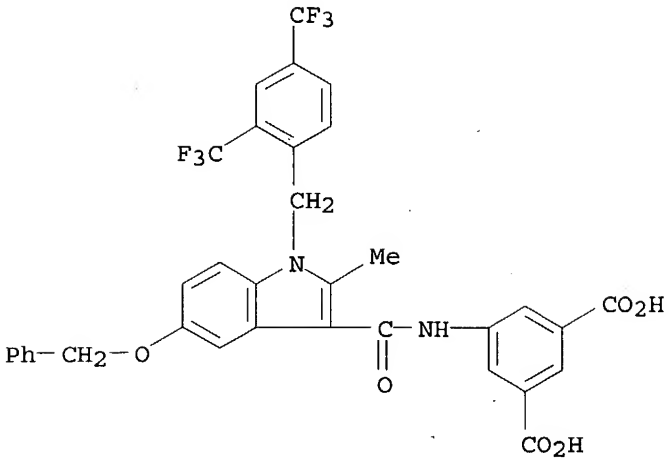


IT **241497-45-0P 241497-83-6P 241497-85-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

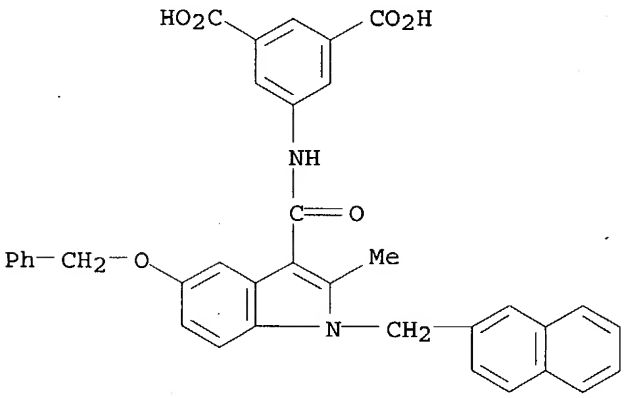
RN 241497-45-0 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-5-(phenylmethoxy)-1H-indol-3-yl]oxoacetyl]amino]- (9CI) (CA INDEX NAME)



RN 241497-83-6 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[1-[[2,4-bis(trifluoromethyl)phenyl]methyl]-2-methyl-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



RN 241497-85-8 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[2-methyl-1-(2-naphthalenylmethyl)-5-(phenylmethoxy)-1H-indol-3-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 14 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:566023 CAPLUS
DOCUMENT NUMBER: 131:199618
TITLE: Preparation of indole derivatives as phospholipase enzyme inhibitors
INVENTOR(S): Seehra, Jasbir S.; Kaila, Neelu; McKew, John C.; Lovering, Frank; Bemis, Jean E.; Xiang, Yibin
PATENT ASSIGNEE(S): Genetics Institute, Inc., USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9943651 | A2 | 19990902 | WO 1999-US3899 | 19990224 <-- |
| WO 9943651 | A3 | 19991216 | | |
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| AU 9927826 | A1 | 19990915 | AU 1999-27826 | | 19990224 <-- |
| BR 9908280 | A | 20001031 | BR 1999-8280 | | 19990224 <-- |
| EP 1056719 | A2 | 20001206 | EP 1999-908379 | | 19990224 <-- |
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| TR 200002446 | T2 | 20001221 | TR 2000-200002446 | | 19990224 <-- |
| JP 2002504539 | T2 | 20020212 | JP 2000-533409 | | 19990224 |
| EE 200000486 | A | 20020215 | EE 2000-486 | | 19990224 |
| NO 2000004220 | A | 20001005 | NO 2000-4220 | | 20000823 <-- |
| HR 2000000552 | A1 | 20010430 | HR 2000-552 | | 20000824 |
| BG 104780 | A | 20011031 | BG 2000-104780 | | 20000919 |
| US 2003153751 | A1 | 20030814 | US 2002-75079 | | 20020508 |
| PRIORITY APPLN. INFO.: | | | US 1998-30062 | A | 19980225 |
| | | | US 1998-100426P | P | 19980225 |
| | | | US 1999-256413 | B2 | 19990224 |
| | | | WO 1999-US3899 | W | 19990224 |
| | | | US 2000-677006 | B1 | 20000929 |

OTHER SOURCE(S): MARPAT 131:199618

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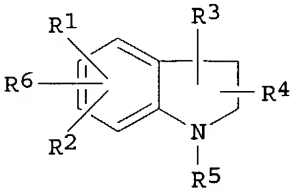


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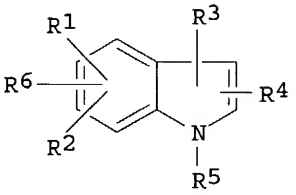


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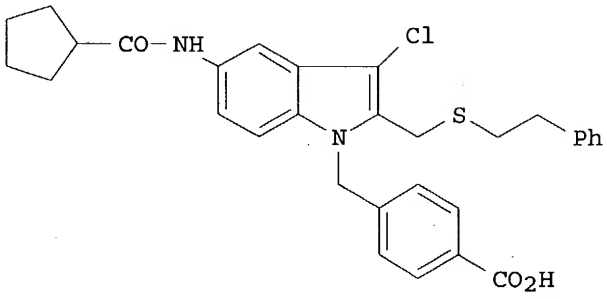



III

AB Indole derivs. (I) and (II) [where R1 and R6 = H, halogen, CF3, OH, C1-10 alkyl, S-C1-10 alkyl, C1-10 alkoxy, CN, NO2, Ph, OPh, SPh, CH2Ph, OCH2Ph, SCH2Ph, or (un)substituted amino, amido, carbamido, sulfonyl, etc.; R2 = H, halogen, CF3, OH, C1-10 alkyl, C1-10 alkoxy, CHO, CN, NO2, (un)substituted amino, SO2-C1-6 alkyl; R3 = H, CF3, C1-6 alkyl, C1-6 alkoxy, (C1-6 alkyl)cycloalkyl, etc.; R4 = C1-6 alkyl, C1-6 alkoxy, alkylcycloalkyl, acyl, etc.; R5 = (un)substituted carboxylic acid, OPO3H2, SO3H, etc.] and pharmaceutically acceptable salts thereof, were prepared by several methods. Thus, Et 5-nitroindole-2-carboxylate was C3-chlorinated in DMF. The alc. was formed by reduction of the ester in a two-step process and was then TBDMS-protected. The TBDMS-protected alc. was N-alkylated with Me 4-(bromomethyl)benzoate, the nitro group reduced to the amine over Pt/C, and the compound reacted with cyclopentylcarbonyl chloride to form the amide. The amide was **treated** with with Ph3PBr2 in CH2Cl2 to convert the protected alc. to the bromide and then reacted with phenethyl mercaptan in the presence of Cs2CO3 followed by NaOH to yield 4-({3-chloro-5-[(cyclopentylcarbonyl)amino]-2-[(phenethylsulfanyl)methyl]-1H-indol-1-yl}methyl)benzoic acid (III). The title compds. are useful as phospholipase enzyme inhibitors, especially cytosolic phospholipase A2 (cPLA2), for **treatment** of inflammatory conditions, particularly where inhibition of production of prostaglandins, leukotrienes, and PAF are all desired (no data).

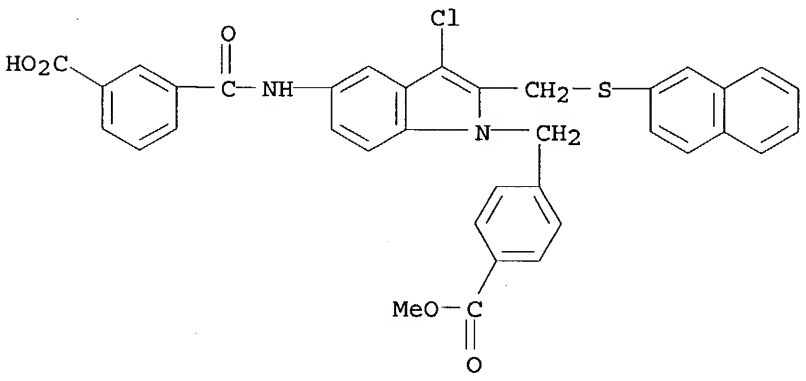
IT **241493-73-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241493-73-2 CAPLUS

CN Benzoic acid, 4-[[5-[(3-carboxybenzoyl)amino]-3-chloro-2-[(2-naphthalenylthio)methyl]-1H-indol-1-yl]methyl]-, 1-methyl ester (9CI) (CA INDEX NAME)



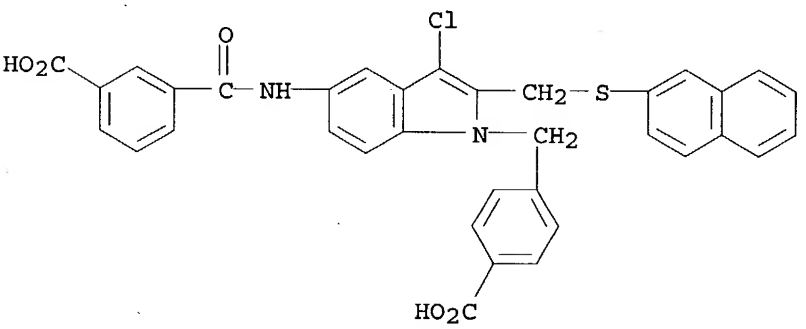
IT **241492-78-4P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of indole derivs. as phospholipase enzyme inhibitors for **treatment** of inflammatory conditions)

RN 241492-78-4 CAPLUS

CN Benzoic acid, 3-[[[1-[(4-carboxyphenyl)methyl]-3-chloro-2-[(2-naphthalenylthio)methyl]-1H-indol-5-yl]amino]carbonyl]- (9CI) (CA INDEX NAME)



L6 ANSWER 15 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:350650 CAPLUS

DOCUMENT NUMBER: 131:18925

TITLE: Preparation of cyclic amine derivatives for inhibition of the action of chemokines such as MIP-1α and/or MCP-1 on target cells

INVENTOR(S): Shiota, Tatsuki; Kataoka, Kenichiro; Imai, Minoru; Tsutsumi, Takaharu; Sudoh, Masaki; Sogawa, Ryo; Morita, Takuya; Hada, Takahiko; Muroga, Yumiko; Takenouchi, Osami; Furuya, Monoru; Endo, Noriaki; Tarby, Christine M.; Moree, Wil A.; Teig, Steven L.

PATENT ASSIGNEE(S): Teijin Ltd., Japan; Combichem, Inc.

SOURCE: PCT Int. Appl., 374 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 9925686 | A1 | 19990527 | WO 1998-US23254 | 19981117 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2309328 | AA | 19990527 | CA 1998-2309328 | 19981117 <-- |
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| AU 744685 | B2 | 20020228 | | |
| EP 1030840 | A1 | 20000830 | EP 1998-957495 | 19981117 <-- |
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| TR 200001399 | T2 | 20001121 | TR 2000-200001399 | 19981117 <-- |
| BR 9814645 | A | 20010731 | BR 1998-14645 | 19981117 |
| EE 200000294 | A | 20010815 | EE 2000-200000294 | 19981117 |
| JP 2001523661 | T2 | 20011127 | JP 2000-521070 | 19981117 |
| RU 2216540 | C2 | 20031120 | RU 2000-112403 | 19981117 |
| HR 2000000214 | A1 | 20011231 | HR 2000-214 | 20000413 |
| NO 2000002486 | A | 20000718 | NO 2000-2486 | 20000512 <-- |
| BG 104441 | A | 20010131 | BG 2000-104441 | 20000516 |
| US 6451842 | B1 | 20020917 | US 2000-554562 | 20000516 |

PRIORITY APPLN. INFO.:

| | | |
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| US 1997-972484 | A | 19971118 |
| US 1998-55285 | A | 19980406 |
| US 1998-133434 | A | 19980813 |
| WO 1998-US23254 | W | 19981117 |

OTHER SOURCE(S): MARPAT 131:18925

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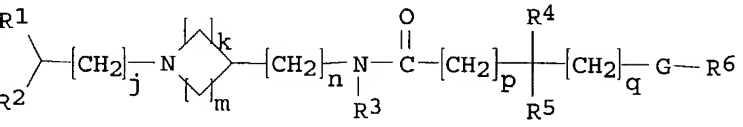

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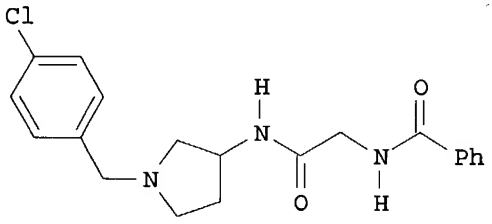


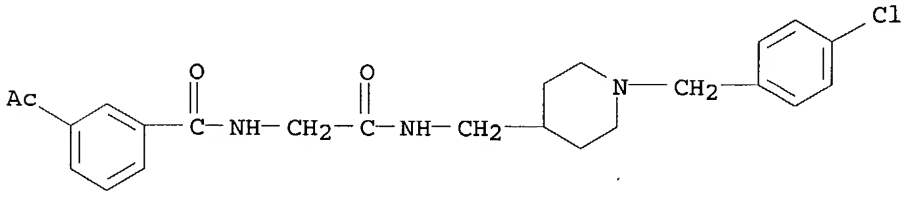
II

AB The title compds. [I; R1 = (un)substituted Ph, cycloalkyl, heteroaryl, etc.; R2 = H, alkyl, alkoxycarbonyl, etc.; j = 0-2; k = 0-2; m = 2-4; n = 0-1; R3 = H, alkyl; R4, R5 = H, OH< Ph, etc.; p = 0-1; q = 0-1; G = CO, SO, CO2, etc.; R6 = Ph, cycloalkyl, cycloalkenyl, etc.] and their pharmaceutically acceptable acid addition salts which inhibit the action of chemokines such as MIP-1α and/or MCP-1 on target cells and may be useful as a therapeutic drug and/or preventative drug in diseases, such as atherosclerosis, **rheumatoid arthritis**, and the like where blood monocytes and lymphocytes infiltrate into tissues, were prepared Thus, reaction of N-benzoylglycine with 3-amino-1-(4-chlorobenzyl)pyrrolidine.2HCl in the presence of 3-ethyl-1-[3-(dimethylaminopropyl)]carbodiimide.HCl, 1-hydroxybenzotriazole and Et3N in CHCl3 afforded 95% II which showed 50-80% inhibition of MIP-1α binding to THP-1 cells at 10 μM.

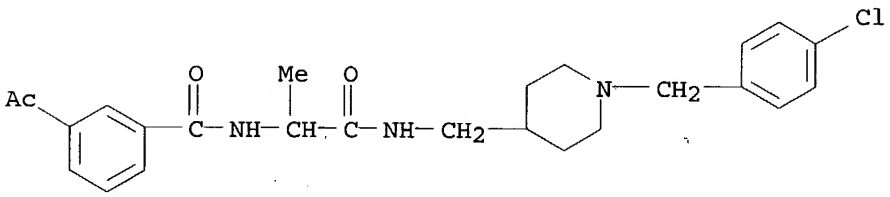
IT **226231-26-1P 226232-13-9P 226232-44-6P**

**226232-66-2P 226232-70-8P 226233-28-9P**
**226233-64-3P 226233-91-6P 226241-34-5P**
**226241-35-6P 226241-39-0P 226241-41-4P**
**226250-69-7P 226250-73-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic amine derivs. for inhibition of the action of chemokines such as MIP-1α and/or MCP-1 on target cells)

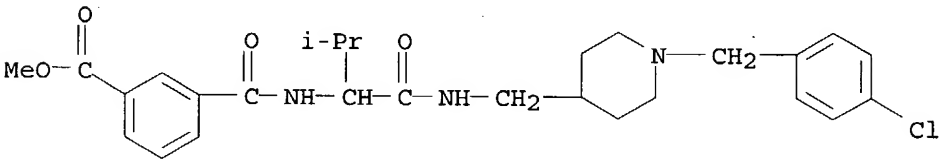
RN 226231-26-1 CAPLUS
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



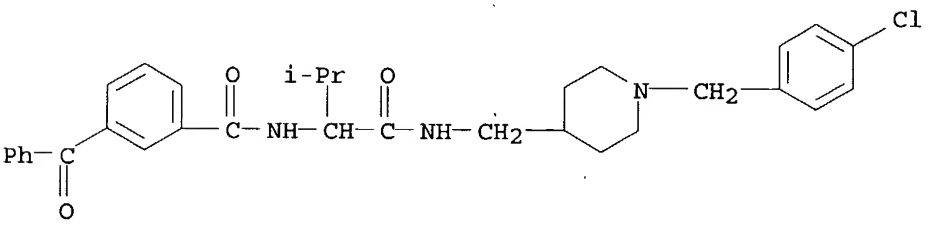
RN 226232-13-9 CAPLUS
CN Benzamide, 3-acetyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-methyl-2-oxoethyl]- (9CI) (CA INDEX NAME)



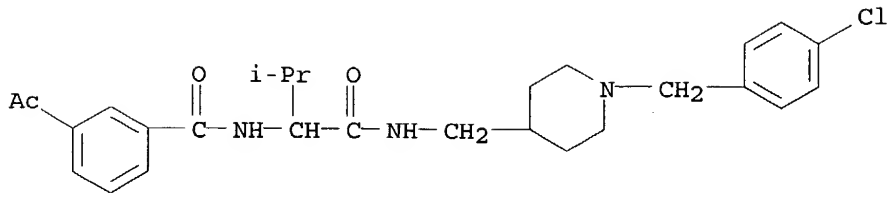
RN 226232-44-6 CAPLUS
CN Benzoic acid, 3-[[[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



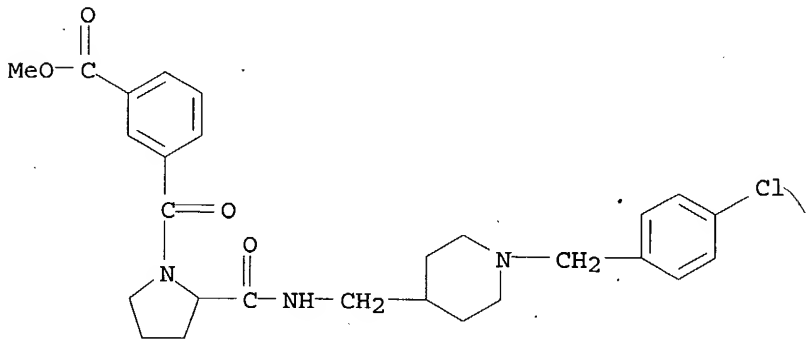
RN 226232-66-2 CAPLUS
CN Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)



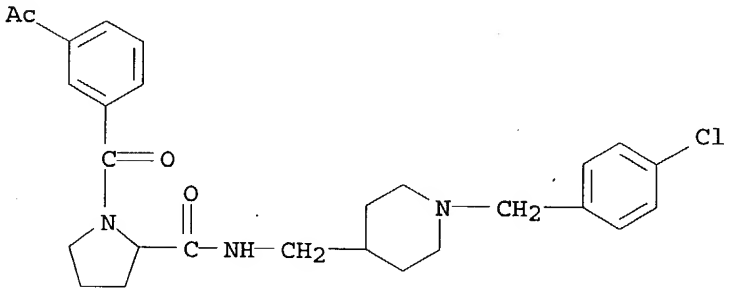
RN 226232-70-8 CAPLUS
CN Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]- (9CI) (CA INDEX NAME)



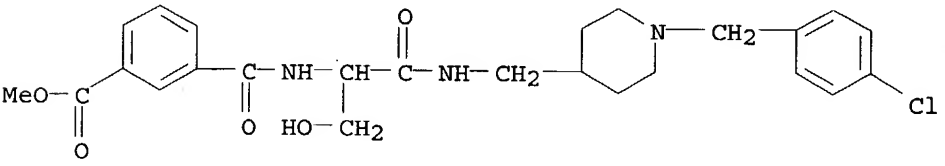
RN 226233-28-9 CAPLUS
CN Benzoic acid, 3-[[2-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-1-pyrrolidinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 226233-64-3 CAPLUS
CN 2-Pyrrolidinecarboxamide, 1-(3-acetylbenzoyl)-N-[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)

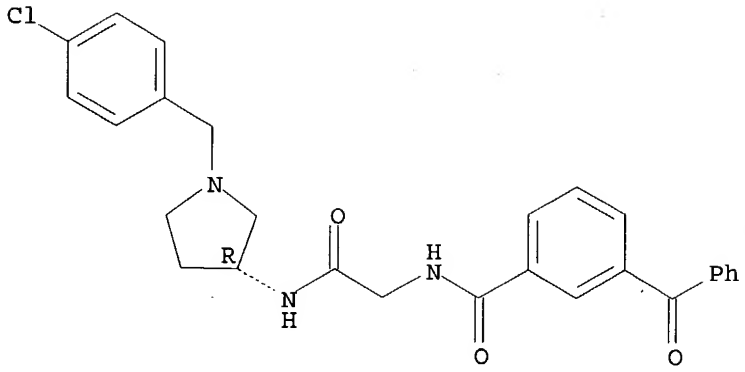


RN 226233-91-6 CAPLUS
CN Benzoic acid, 3-[[[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-1-(hydroxymethyl)-2-oxoethyl]amino]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



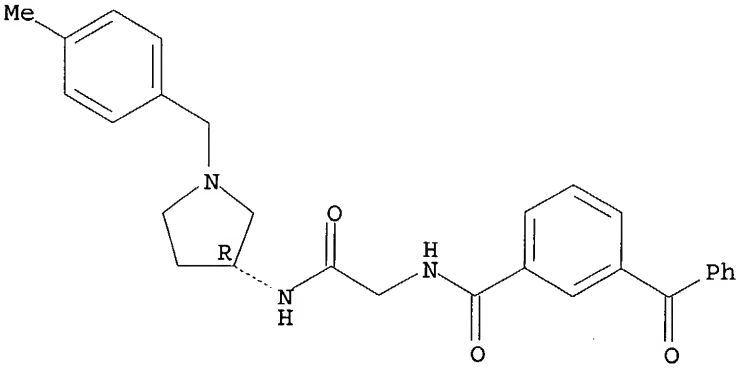
RN 226241-34-5 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-chlorophenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



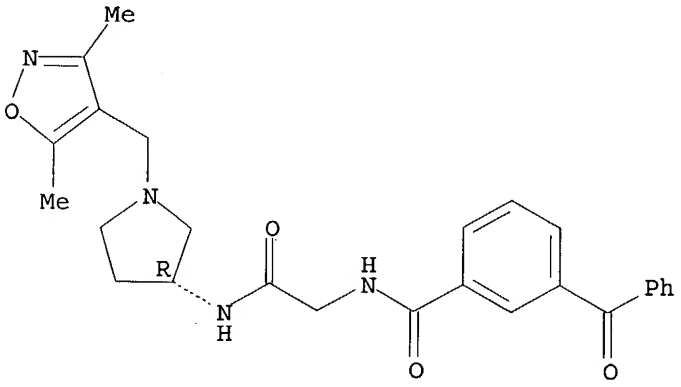
RN 226241-35-6 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(4-methylphenyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

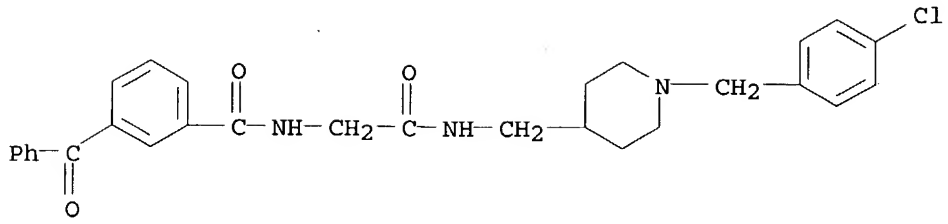


RN 226241-39-0 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[(3R)-1-[(3,5-dimethyl-4-isoxazolyl)methyl]-3-pyrrolidinyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



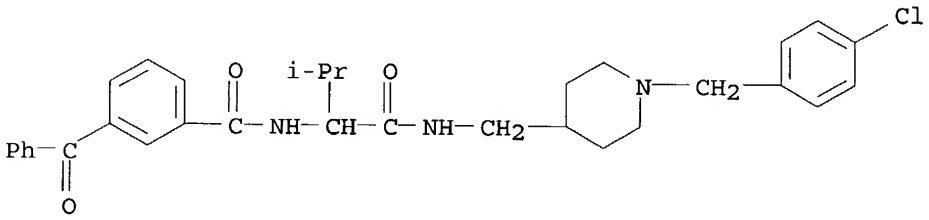
RN 226241-41-4 CAPLUS
CN Benzamide, 3-benzoyl-N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 226250-69-7 CAPLUS
CN Benzamide, 3-benzoyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

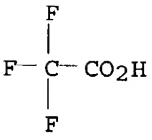
CM 1

CRN 226232-66-2
CMF C32 H36 Cl N3 O3



CM 2

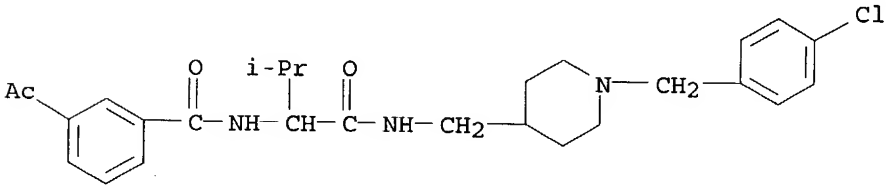
CRN 76-05-1
CMF C2 H F3 O2



RN 226250-73-3 CAPLUS
CN Benzamide, 3-acetyl-N-[1-[[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]carbonyl]-2-methylpropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

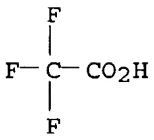
CRN 226232-70-8
CMF C27 H34 Cl N3 O3



CM 2

CRN 76-05-1

CMF C2 H F3 O2



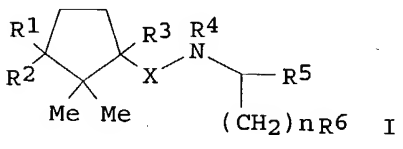
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:27805 CAPLUS
DOCUMENT NUMBER: 130:95843
TITLE: Preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion
INVENTOR(S): Lobl, Thomas J.; Rishton, Gil; Teegarden, Bradley; Polinsky, Alex; Yamagishi, Masafumi; Tanis, Steven P.; Fisher, Jed F.; Thomas, Edward W.; Chrusciel, Robert A.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 342 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9858902 | A1 | 19981230 | WO 1998-US13064 | 19980623 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9881633 | A1 | 19990104 | AU 1998-81633 | 19980623 <-- |
| EP 991619 | A1 | 20000412 | EP 1998-931521 | 19980623 <-- |
| EP 991619 | B1 | 20030910 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| JP 2001517246 | T2 | 20011002 | JP 1999-504997 | 19980623 |
| US 6482849 | B1 | 20021119 | US 1998-102584 | 19980623 |
| AT 249421 | E | 20030915 | AT 1998-931521 | 19980623 |
| PT 991619 | T | 20040227 | PT 1998-931521 | 19980623 |
| ES 2206953 | T3 | 20040516 | ES 1998-931521 | 19980623 |
| US 2003130349 | A1 | 20030710 | US 2002-193137 | 20020712 |
| US 6596752 | B1 | 20030722 | | |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1997-50515P | P | 19970623 |
| | US 1998-102584 | A3 | 19980623 |
| | WO 1998-US13064 | W | 19980623 |

OTHER SOURCE(S): MARPAT 130:95843
GI



I

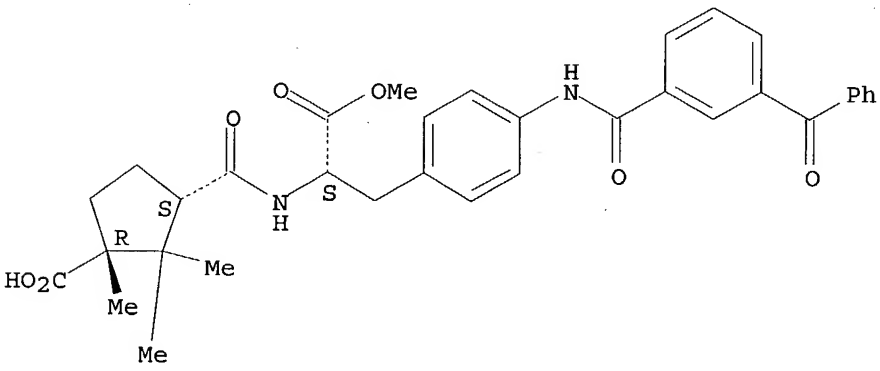
AB Title compds. [I; n = 0, 1; R1 = H, CH3; R2 = CN, CO2H, CONH2, CONHOCH2Ph, NHCOOCH2Ph, etc.; R3 = H, CH3; X = CH, CO; R4 = H, alkyl; R5 = CO2H, CONH2, COOR, etc.; R = alkyl; R6 = aryl, heteroaryl, arylcarbonyl, aarylcarbonylaminoalkyl, etc.], a pharmaceutically acceptable salt, a stereoisomer thereof are prepared as inhibitors of α4β1 mediated adhesion to either VCAM or CS-1 and which can be used for **treating** or preventing α4β1 adhesion mediated conditions in human such as inflammatory diseases. Thus, (1S-cis)- N-[(3-carboxy-2,2,3-trimethylcyclopentyl)carbonyl]-O-(phenylmethyl)-L-tyrosine was prepared and assayed for inhibition of β1-mediated cell adhesion in vitro.

IT **219494-75-4P 219494-76-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclopentylcarbonylamino acid as inhibitors of α4β1 mediated cell adhesion)

RN 219494-75-4 CAPLUS

CN L-Phenylalanine, 4-[(3-benzoylbenzoyl)amino]-N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl]-, α-methyl ester (9CI) (CA INDEX NAME)

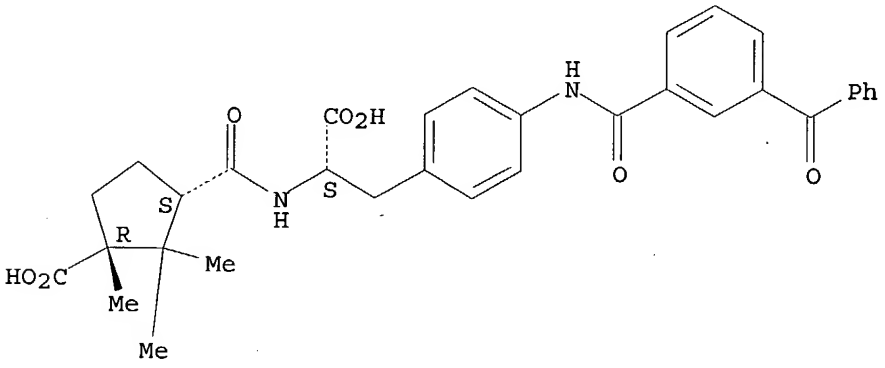
Absolute stereochemistry.



RN 219494-76-5 CAPLUS

CN L-Phenylalanine, 4-[(3-benzoylbenzoyl)amino]-N-[[(1S,3R)-3-carboxy-2,2,3-trimethylcyclopentyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:693417 CAPLUS

DOCUMENT NUMBER: 129:343326

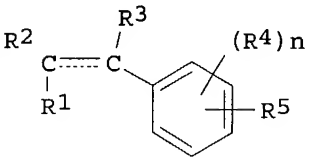
TITLE: Preparation of benzenes as protein kinase C inhibitors

INVENTOR(S): Mori, Toyoki; Tominaga, Michiaki; Tabusa, Fujio; Ei, Kazuyoshi; Nakaya, Kenji; Takemura, Isao; Shinohara, Tomokazu; Tanada, Yoshihisa; Yamauchi, Takahito;

| | |
|---|---|
| | Kitano, Kazuyoshi |
| PATENT ASSIGNEE(S): | Otsuka Pharmaceutical Co., Ltd., Japan |
| SOURCE: | Jpn. Kokai Tokkyo Koho, 359 pp. |
| | CODEN: JKXXAF |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | Japanese |
| FAMILY ACC. NUM. COUNT: | 1 |
| PATENT INFORMATION: | |

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 10287634 | A2 | 19981027 | JP 1997-110527 | 19970411 <-- |
| PRIORITY APPLN. INFO.: | | | JP 1997-110527 | 19970411 |
| OTHER SOURCE(S): | MARPAT 129:343326 | | | |

GI



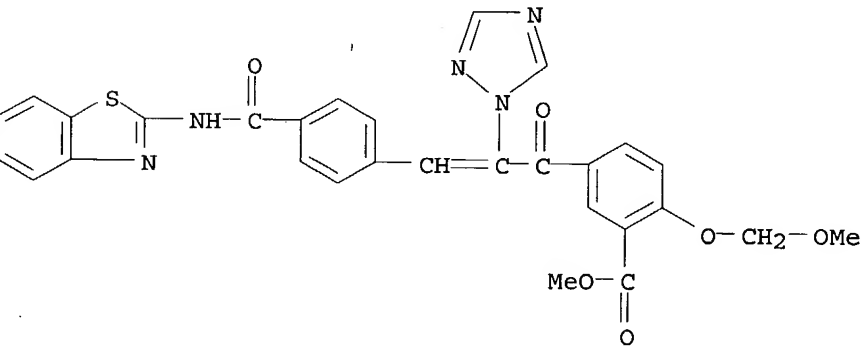
I


AB Benzenes I [R1 = 5- to 6-membered (un)substituted unsatd. heterocyclyl having 1-4 N, O, or S; cyano, carboxylalkyl, alkoxycarbonyl, H, Bz, (un)substituted amido, etc.; R2 = (un)substituted Bz, (un)substituted 1,2,3,4-tetrahydroquinolinylcarbonyl, pyridylcarbonyl, (un)substituted phenoxycarbonyl, etc.; R3 = H, lower alkyl, PhS, (un)substituted lower alkylthio, cycloalkylthio, cyano, etc.; R4 = H, (un)substituted lower alkyl, lower alkoxy, (un)substituted aminoalkylene, (un)substituted aminoalkylenyloxy; R5 = substituted alkenyl, phenylthioureidocarbonyl, pyrimidylaminocarbonylalkoxy, etc.; n = 1-3; the dot line may be double bond] or their salts are prepared I are useful for prevention and **treatment** of chronic **rheumatoid arthritis**, systemic lupus erythematosus, atopic dermatitis, **heart failure**, allergy, multiple sclerosis, tumor, Alzheimer-type dementia, etc. Condensation of 250 mg 2-(benzoylmethyl)pyridine with 300 mg 4-[(2-benzothiazolyl)aminocarbonyl]benzaldehyde in C6H6 for 10 h gave 0.3 g 2-[4-[2-benzoyl-2-(2-pyridyl)vinyl]benzoylamino]benzothiazole.

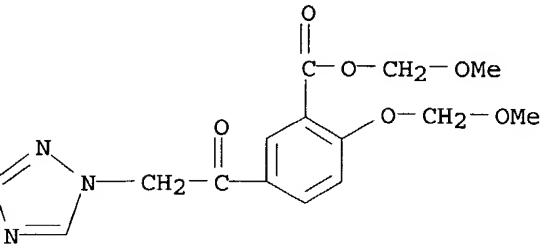

IT **215504-19-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)

RN 215504-19-1 CAPLUS

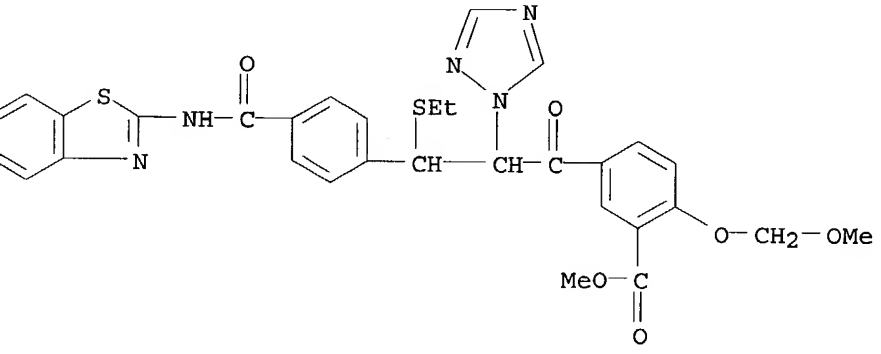
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)



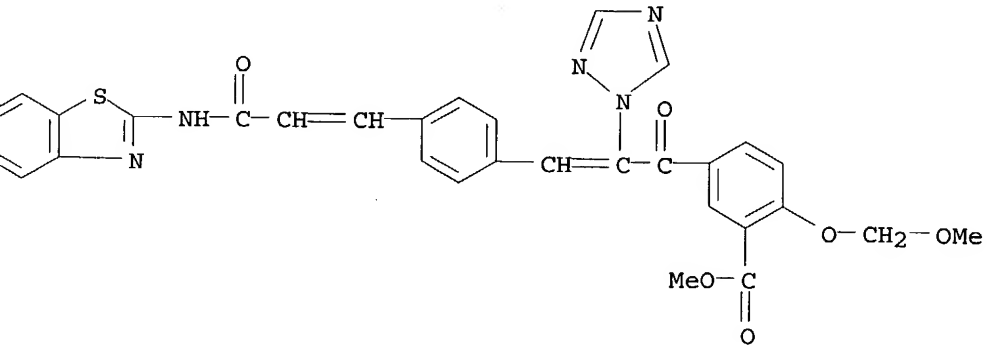
IT **215503-79-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)
RN 215503-79-0 CAPLUS
CN Benzoic acid, 2-(methoxymethoxy)-5-(1H-1,2,4-triazol-1-ylacetyl)-, methoxymethyl ester (9CI) (CA INDEX NAME)



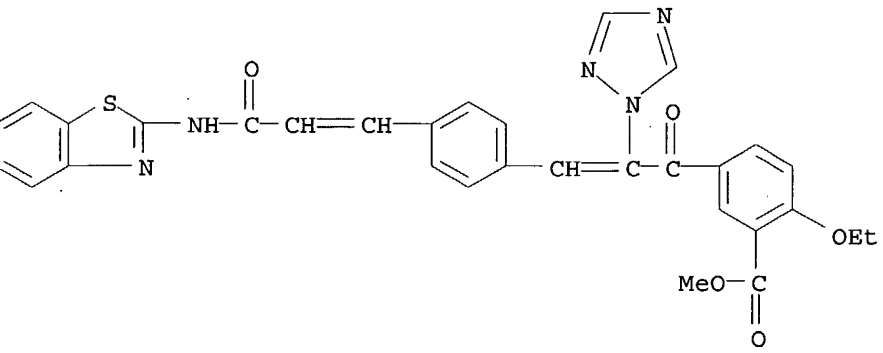
IT **215504-20-4P 215504-43-1P 215504-55-5P**
**215504-56-6P 215504-69-1P 215504-93-1P**
**215504-94-2P 215504-96-4P 215505-17-2P**
**215505-94-5P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzenes as protein kinase C inhibitors for **treatment** of diseases)
RN 215504-20-4 CAPLUS
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-3-(ethylthio)-1-oxo-2-(1H-1,2,4-triazol-1-yl)propyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)



RN 215504-43-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(methoxymethoxy)-, methyl ester (9CI) (CA INDEX NAME)

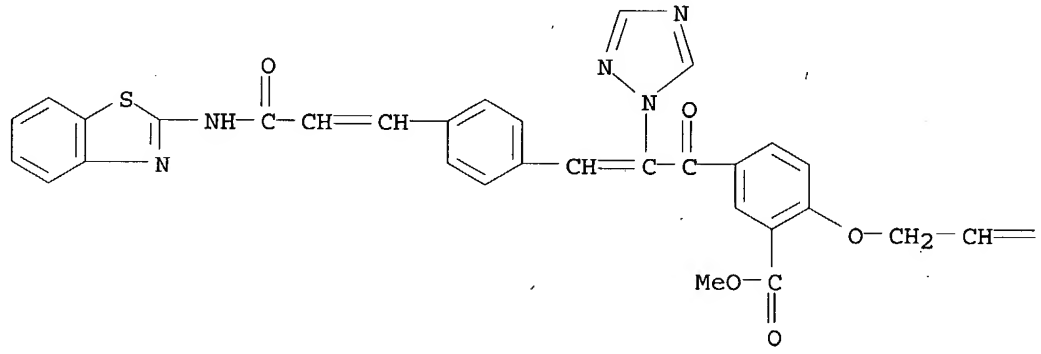


RN 215504-55-5 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-, methyl ester (9CI) (CA INDEX NAME)



RN 215504-56-6 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-(2-propenyloxy)-, methyl ester (9CI) (CA INDEX NAME)

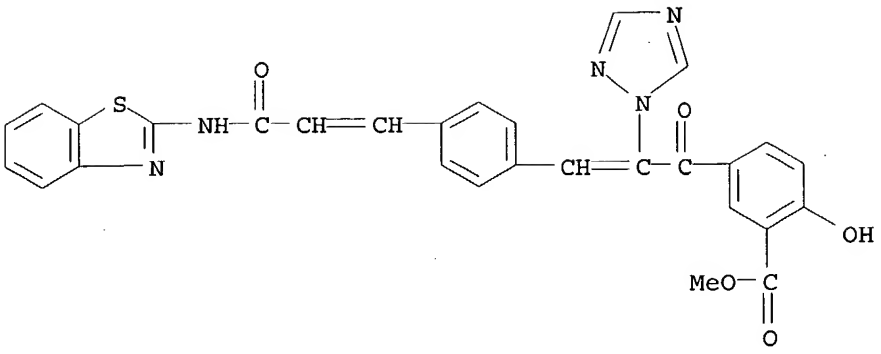
PAGE 1-A



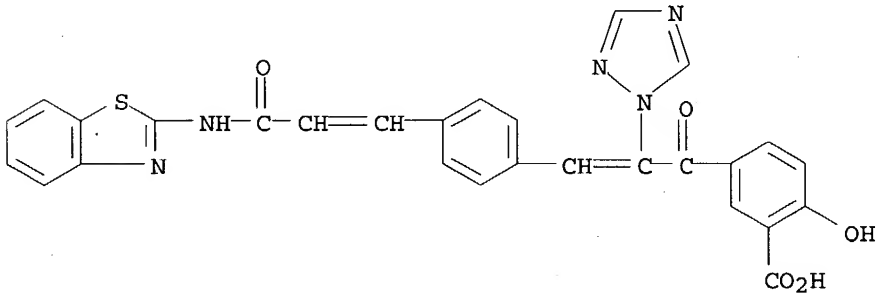
PAGE 1-B

$= CH_2$

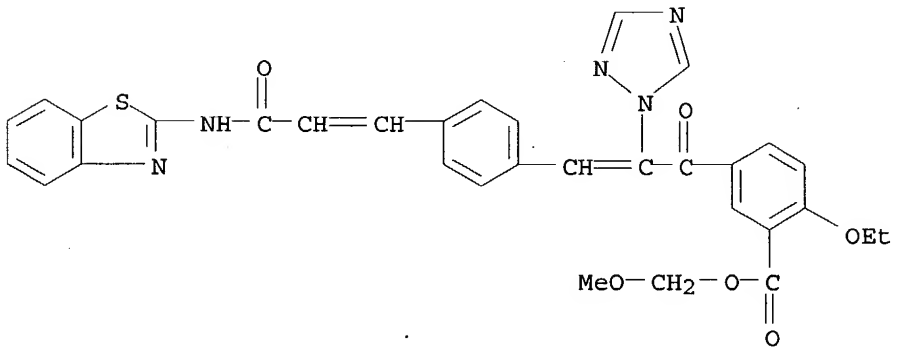
RN 215504-69-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



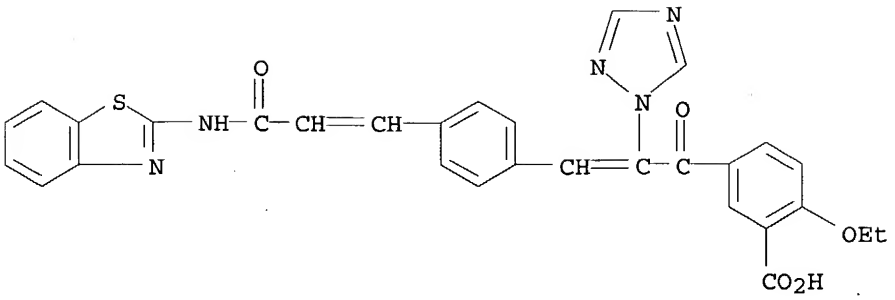
RN 215504-93-1 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy- (9CI) (CA INDEX NAME)



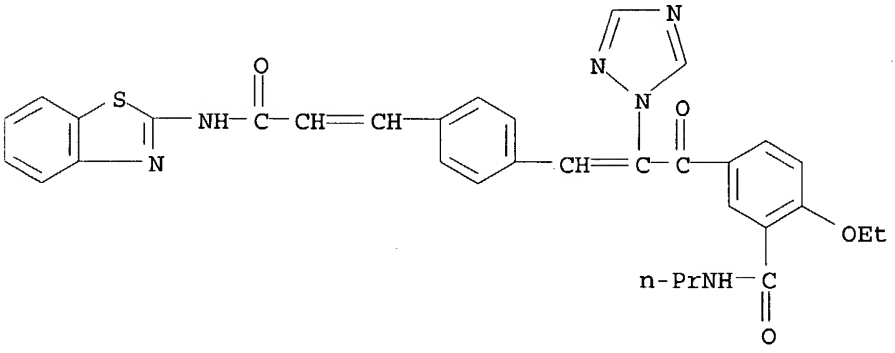
RN 215504-94-2 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-, methoxymethyl ester (9CI) (CA INDEX NAME)



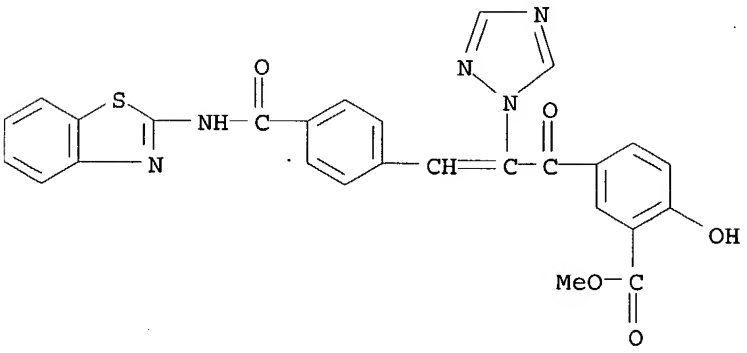
RN 215504-96-4 CAPLUS
CN Benzoic acid, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy- (9CI) (CA INDEX NAME)



RN 215505-17-2 CAPLUS
CN Benzamide, 5-[3-[4-[3-(2-benzothiazolylamino)-3-oxo-1-propenyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-ethoxy-N-propyl- (9CI) (CA INDEX NAME)



RN 215505-94-5 CAPLUS
CN Benzoic acid, 5-[3-[4-[(2-benzothiazolylamino)carbonyl]phenyl]-1-oxo-2-(1H-1,2,4-triazol-1-yl)-2-propenyl]-2-hydroxy-, methyl ester (9CI) (CA INDEX NAME)



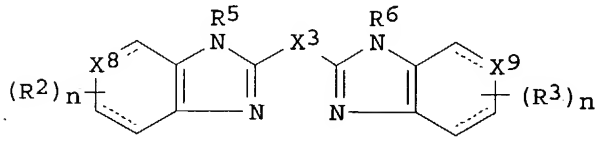
L6 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682372 CAPLUS
DOCUMENT NUMBER: 129:316232
TITLE: Preparation of compounds and compositions for **treating** diseases associated with serine protease, particularly tryptase, activity
INVENTOR(S): Church, Timothy J.; Cutshall, Neil Scott; Gangloff, Anthony R.; Jenkins, Thomas E.; Linsell, Martin S.; Litvak, Joane; Rice, Kenneth D.; Spencer, Jeffrey R.; Wang, Vivian R.
PATENT ASSIGNEE(S): Axys Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9845275 | A1 | 19981015 | WO 1997-US21849 | 19971201 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| AU 9858950 | A1 | 19981030 | AU 1998-58950 | 19971201 <-- |
| AU 752064 | B2 | 20020905 | | |
| CN 1251579 | A | 20000426 | CN 1997-182098 | 19971201 <-- |
| EE 9900477 | A | 20000615 | EE 1999-477 | 19971201 <-- |
| EE 4055 | B1 | 20030616 | | |
| EP 1019382 | A1 | 20000719 | EP 1997-954520 | 19971201 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| NZ 500029 | A | 20010223 | NZ 1997-500029 | 19971201 |
| JP 2001519806 | T2 | 20011023 | JP 1998-542739 | 19971201 |
| MX 9909006 | A | 20000831 | MX 1999-9006 | 19991001 <-- |
| NO 9904858 | A | 19991206 | NO 1999-4858 | 19991006 <-- |
| LV 12495 | B | 20010120 | LV 1999-153 | 19991102 |
| LT 4704 | B | 20000925 | LT 1999-131 | 19991105 <-- |
| US 2001053779 | A1 | 20011220 | US 2001-874412 | 20010604 |
| US 6562854 | B2 | 20030513 | | |
| US 2003212120 | A1 | 20031113 | US 2003-401415 | 20030314 |

| | | | |
|---|---|---|---|
| PRIORITY APPLN. INFO.: | US 1997-833674 | A | 19970407 |
| | US 1994-357491 | B2 | 19941214 |
| | US 1997-980515 | A1 | 19971201 |
| | WO 1997-US21849 | W | 19971201 |
| | US 2001-874412 | A1 | 20010604 |

OTHER SOURCE(S): CASREACT 129:316232; MARPAT 129:316232
GI




I

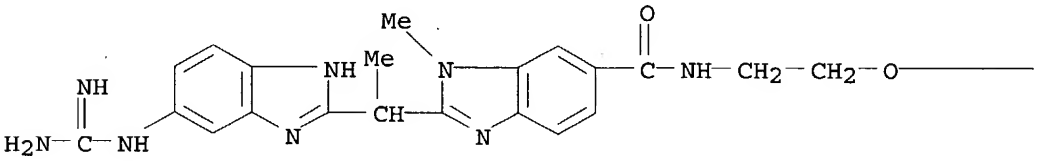
AB A preferred aspect of the invention are compds. of Formula [I; in which: the dashed lines independently represent optional bonds; each R2 independently is (C1-6)alkyl, (C1-6)alkyloxy, halo or hydroxy; each R3 independently is (C1-6)alkyl, (C1-6)alkyloxy, halo or hydroxy; X3 is -C(O)- or -CR7R8-, X8 is -CH(R1)n1- or -C(R1)n1=, wherein R1 is amino(N1-4)azolidinyl, amino(N1-4)azolyl, (N1-4)azolidinyl, (N1-4)azolyl, etc.; X8 is -N= or -NH(R1)n1-, wherein R1 is -C(NR9)R9, -C(NH)NHR10 or -C(NH)NR10R10, wherein R9 independently is hydrogen or (C1-6)alkyl and each R10 independently is (C1-6)alkyl; and X9 is -CH(R4)- or -C(R4)=, wherein R4 is -R12, -OR12, -N(R13)R12, etc.; wherein R4 is -C(O)R12, -C(O)OR12, -C(O)N(R13)R12, etc.; R12 is cyano, guanidino, halo, alkyl, etc.; R13 is hydrogen, alkyl; R5 is hydrogen or (C1-4)alkyl, R6 is hydrogen or (C1-4) alkyl; R7 is hydrogen, methyl; R8 is hydrogen Me, hydroxy; n = 0-4]. The compds., compns. and methods are effective for the prevention and **treatment** of inflammatory diseases associated with the respiratory tract, such as asthma and allergic rhinitis, as well as other types of immunomediated inflammatory disorders, such as **rheumatoid arthritis**, conjunctivitis and inflammatory bowel disease, various dermatol. conditions, as well as certain viral

conditions. The compds. comprise potent and selective inhibitors of the mast-cell protease tryptase. The compns. for **treating** these conditions include oral, inhalant, topical and parenteral prepns. as well as devices comprising such prepns.

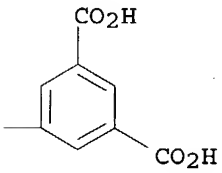
IT **214781-30-3P 214781-74-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of arenoimidazoles for **treating** human inflammatory disorder)

RN 214781-30-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[2-[[[2-[1-[5-[(aminoiminomethyl)amino]-1H-benzimidazol-2-yl]ethyl]-1-methyl-1H-benzimidazol-6-yl]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)

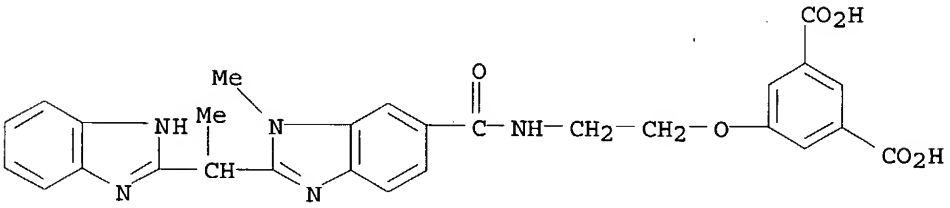
PAGE 1-A



PAGE 1-B



RN 214781-74-5 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[2-[[[2-[1-(1H-benzimidazol-2-yl)ethyl]-1-methyl-1H-benzimidazol-6-yl]carbonyl]amino]ethoxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

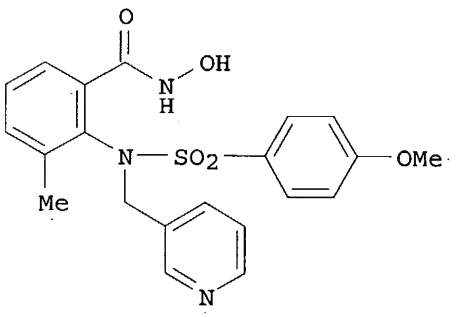
L6 ANSWER 19 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:251153 CAPLUS
DOCUMENT NUMBER: 128:308308
TITLE: The preparation and use of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors
INVENTOR(S): Levin, Jeremy Ian; Du Mila, T.; Venkatesan, Aranapakam Mudumbai; Nelson, Frances Christy; Zask, Arie; Gu, Yansong
PATENT ASSIGNEE(S): American Cyanamid Company, USA
SOURCE: PCT Int. Appl., 164 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9816503 | A2 | 19980423 | WO 1997-US18280 | 19971008 <-- |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| CA 2268894 | AA | 19980423 | CA 1997-2268894 | 19971008 <-- |
| AU 9851458 | A1 | 19980511 | AU 1998-51458 | 19971008 <-- |
| AU 731737 | B2 | 20010405 | | |
| EP 938471 | A1 | 19990901 | EP 1997-946246 | 19971008 <-- |
| EP 938471 | B1 | 20011212 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| BR 9712525 | A | 19991019 | BR 1997-12525 | 19971008 <-- |
| CN 1240429 | A | 20000105 | CN 1997-180613 | 19971008 <-- |
| JP 2001504809 | T2 | 20010410 | JP 1998-518448 | 19971008 |
| AT 210637 | E | 20011215 | AT 1997-946246 | 19971008 |
| ES 2166102 | T3 | 20020401 | ES 1997-946246 | 19971008 |
| PT 938471 | T | 20020531 | PT 1997-946246 | 19971008 |
| ZA 9709233 | A | 19990415 | ZA 1997-9233 | 19971015 <-- |
| TW 410220 | B | 20001101 | TW 1997-86114187 | 19971015 <-- |
| KR 2000049196 | A | 20000725 | KR 1999-703294 | 19990415 <-- |
| HK 1021178 | A1 | 20020404 | HK 2000-100090 | 20000106 |

PRIORITY APPLN. INFO.: US 1996-732631 A 19961016
WO 1997-US18280 W 19971008

OTHER SOURCE(S): MARPAT 128:308308
GI




II

AB The invention relates to novel, low mol. weight, non-peptide inhibitors of matrix metalloproteinases (e.g. gelatinases, stromelysins and collagenases) and TNF-α converting enzyme (TACE, tumor necrosis factor-α converting enzyme). The compds. are useful for the **treatment** of diseases in which these enzymes are implicated such as arthritis, tumor growth and metastasis, angiogenesis, tissue ulceration, abnormal wound healing, periodontal disease, bone disease, proteinuria, aneurysmal aortic disease, degenerative cartilage loss following traumatic joint injury, demyelinating diseases of the nervous system, graft rejection, cachexia, anorexia, inflammation, fever, insulin resistance, septic shock, congestive **heart failure**, inflammatory disease of the central nervous system, inflammatory bowel disease, HIV infection, age related macular degeneration, diabetic retinopathy, proliferative vitreoretinopathy, retinopathy of prematurity, ocular inflammation, keratoconus, Sjogren's syndrome, myopia, ocular tumors, and ocular angiogenesis/neovascularization. The invention compds. are represented by the formula ZSO2N(CH2R7)ACONHOH [I; A = (un)substituted

Ph or naphthyl; Z = (un)substituted aryl, heteroaryl, or benzo-fused heteroaryl; R7 = H, (un)substituted alk(en/yn)yl, Ph, naphthyl, 5- or 6-membered heteroaryl, cycloalkyl, or cycloheteroalkyl; or R7CH2NA forms a non-aromatic 1,2-benzo-fused 7- to 10-membered heterocyclic ring with an optional addition benzo fusion; where the hydroxamic acid moiety and the sulfonamido moiety are bonded to adjacent carbons on group A], and include pharmaceutically acceptable salts, optical isomers, and diastereomers. Prepns. of over 400 compds., including I and their intermediates, are given. For instance, 2-[(4-methoxybenzenesulfonyl)amino]-3-methylbenzoic acid Me ester (preparation given) was N-alkylated by 3-picolyl chloride-HCl (83%), followed by hydrolysis of the ester with LiOH in aqueous THF (100%), activation with oxalyl chloride, and hydroxamidation with NH2OH.HCl (51%), to give title compound II. At 50 mg/kg/day in rats with cartilage implants, II gave 44.6% inhibition of cartilage weight loss, and 51.2% inhibition of cartilage collagen loss.

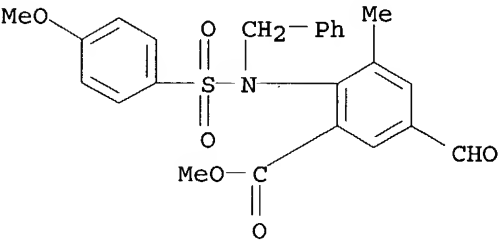
IT **206549-41-9P 206549-42-0P 206549-43-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors)

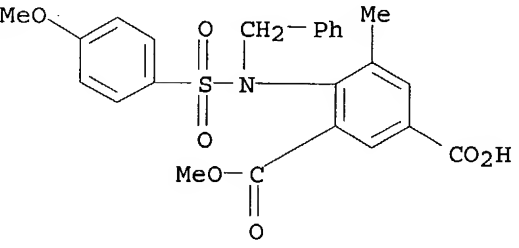
RN 206549-41-9 CAPLUS

CN Benzoic acid, 5-formyl-2-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-3-methyl-, methyl ester (9CI) (CA INDEX NAME)



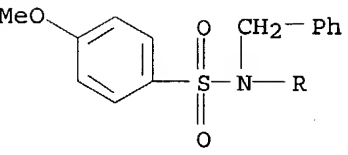

RN 206549-42-0 CAPLUS

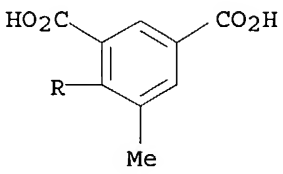
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, 3-methyl ester (9CI) (CA INDEX NAME)




RN 206549-43-1 CAPLUS

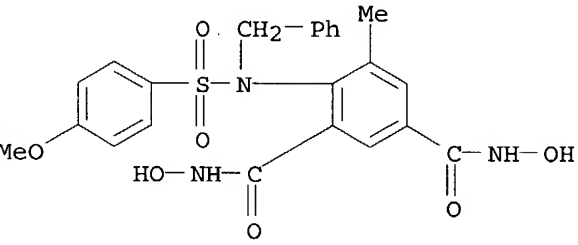
CN 1,3-Benzenedicarboxylic acid, 4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



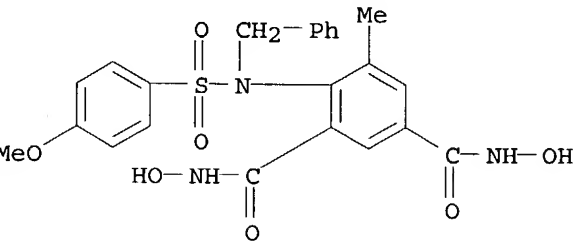


IT **206549-44-2P 206549-45-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of ortho-sulfonamido aryl hydroxamic acids as matrix metalloproteinase and TACE inhibitors)

RN 206549-44-2 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl- (9CI) (CA INDEX NAME)



RN 206549-45-3 CAPLUS
CN 1,3-Benzenedicarboxamide, N,N'-dihydroxy-4-[[(4-methoxyphenyl)sulfonyl](phenylmethyl)amino]-5-methyl-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L6 ANSWER 20 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:310799 CAPLUS
DOCUMENT NUMBER: 126:293363
TITLE: Preparation of 2-phenylsulfonyl- and 2-(heterocyclylsulfonyl)quinazoline derivatives as chymase inhibitors
INVENTOR(S): Fukami, Harukazu; Ito, Akiko; Niwata, Shinjiro; Kakutani, Saki; Sumida, Motoo; Kiso, Yoshinobu

PATENT ASSIGNEE(S): Suntory Limited, Japan; Fukami, Harukazu; Ito, Akiko; Niwata, Shinjiro; Kakutani, Saki; Sumida, Motoo; Kiso, Yoshinobu

SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

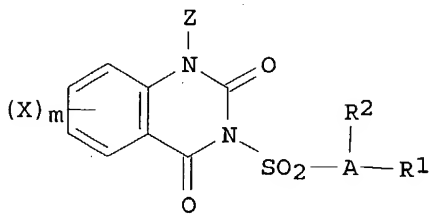
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9711941 | A1 | 19970403 | WO 1996-JP2830 | 19960927 <-- |
| W: JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 795548 | A1 | 19970917 | EP 1996-932039 | 19960927 <-- |
| EP 795548 | B1 | 20020703 | | |
| R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| ES 2175127 | T3 | 20021116 | ES 1996-932039 | 19960927 |
| US 5814631 | A | 19980929 | US 1997-849114 | 19970528 <-- |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| JP 1995-285437 | A | 19950928 |
| JP 1996-116557 | A | 19960510 |
| WO 1996-JP2830 | W | 19960927 |

OTHER SOURCE(S): MARPAT 126:293363

GI



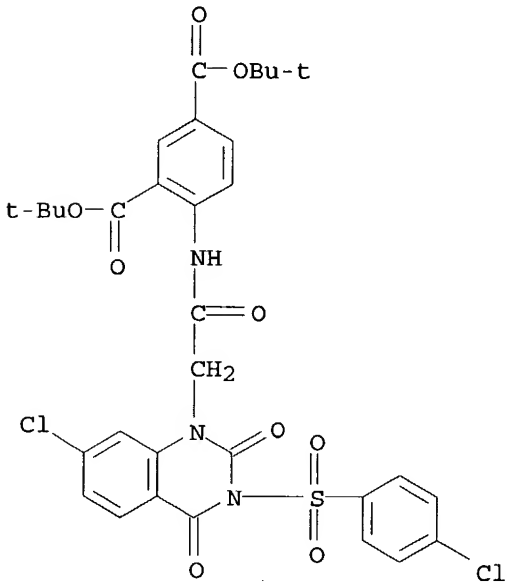
I

AB Quinazoline derivs. represented by general formula [I; group A = benzene, pyridine, pyrrole, or pyrazole ring; m = 0-2; X = OH, NO2, halo, C1-4 (halo)alkyl, or (halo)alkoxy, C7-12 aralkyloxy; X = group to form a naphthalene or quinoline ring together with the benzene ring to which X is attached; R1, R2 = H, halo, C1-4 (halo)alkyl, NO2, cyano, pyrazolyl, tetrazolyl, C1-4 alkyl, CO2H, allyloxycarbonyl, C1-4 (un)substituted alkoxy; or R1 and R2 together with the benzene ring represent a naphthalene or quinoline ring; Z = H, C1-4 (halo)alkyl, C2-5 alkenyl, (un)substituted aralkyl, aromatic heterocyclylalkyl, C1-4 alkoxycarbonylmethyl, allyloxycarbonylmethyl, (1° or 2° amino)carbonylmethyl, (un)substituted aralkyloxymethyl; proviso given] or pharmacol. acceptable salts thereof are prepared They are useful as preventives/remedies for cardiac and circulatory diseases (e.g. hypertension or **heart failure**) caused by abnormal overprodn. of angiotensin II. Thus, a quinazolinedione derivative (II; R = H) (preparation given) was condensed with 3-(diethylamino)-1,5-dihydro-2,4,3-benzodioxaphosphepine in the presence of tetrazole in DMF, followed by oxidation with m-chloroperbenzoic acid in CH2Cl2 and hydrogenolysis over 10% Pd-C in dioxane under H atmospheric to give II [R = P(O)(OH)2]. II (R = H) and II [R = P(O)(OH)2] showed IC50 of 0.060 and 0.025 μM, resp., for inhibiting human heart chymase. The title compds. I also inhibited cathepsin G and chymotrypsin. Formulation examples containing I were given.

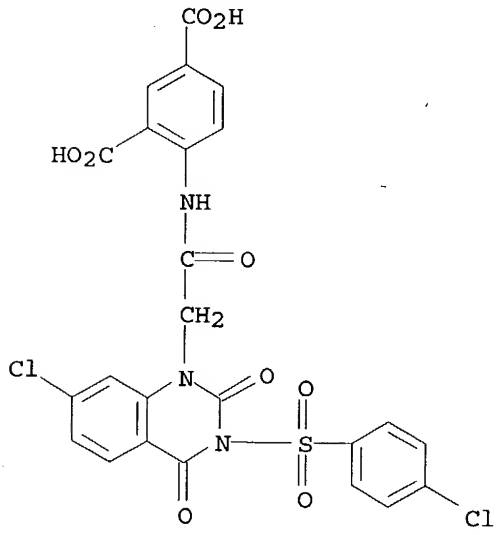
IT **189062-20-2P 189062-21-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-phenylsulfonyl- and N-(heterocyclylsulfonyl)quinazoline derivs. as chymase inhibitors for **treating** heart or circulatory diseases)

RN 189062-20-2 CAPLUS

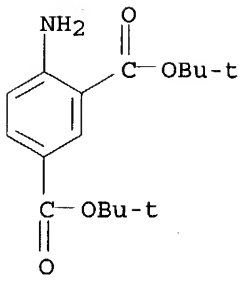
CN 1,3-Benzenedicarboxylic acid, 4-[[[7-chloro-3-[(4-chlorophenyl)sulfonyl]-3,4-dihydro-2,4-dioxo-1(2H)-quinazolinyl]acetyl]amino]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



RN 189062-21-3 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-[[[7-chloro-3-[(4-chlorophenyl)sulfonyl]-3,4-dihydro-2,4-dioxo-1(2H)-quinazolinyl]acetyl]amino]- (9CI) (CA INDEX NAME)



IT **189062-98-4**, 2,4-Di-tert-butoxycarbonylaniline
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of N-phenylsulfonyl- and N-(heterocyclylsulfonyl)quinazoline derivs. as chymase inhibitors for **treating** heart or circulatory diseases)
RN 189062-98-4 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 4-amino-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



L6 ANSWER 21 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:483335 CAPLUS
DOCUMENT NUMBER: 121:83335
TITLE: Preparation of substituted benzimidazoles useful as angiotensin II receptor antagonists
INVENTOR(S): Franz, Robert G.; Weinstock, Joseph
PATENT ASSIGNEE(S): SmithKline Beecham Corp., USA
SOURCE: U.S., 19 pp. Cont.-in-part of U.S. Ser No. 509,268, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5294631 | A | 19940315 | US 1992-937885 | 19921013 <-- |
| WO 9116313 | A1 | 19911031 | WO 1991-US2396 | 19910408 <-- |
| W: AU, CA, JP, KR, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |

PRIORITY APPLN. INFO.: US 1990-509268 19900413
WO 1991-US2396 19910408

OTHER SOURCE(S): MARPAT 121:83335
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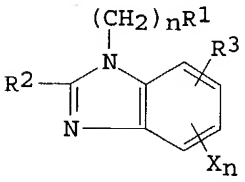
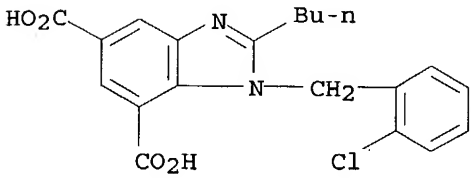


I

AB The preparation of title compds. I [R1 = CONHCH(Y)(CH2)naryl, CONHCH(Y)(CH2)nheteroaryl, substituted Ph, etc.; R2 = H, C2-10 alkyl, C3-10 alkenyl, C3-6 cycloalkyl, etc.; R3 = (CH2)nY, CH:CY(CH2)naryl, CH:CY(CH2)nheteroaryl, (CH2)nCONHCHY(CH2)naryl, etc.; Y = substituted carboxy, tetrazol-5-yl; X = halo, perfluoroalkyl, C1-6 alkyl, etc.; n = 0-2], useful in regulating hypertension and in the **treatment** of congestive **heart failure**, renal failure, and glaucoma, pharmaceutical compns. including these antagonists, and methods of using these compds. to produce angiotensin II receptor antagonism in mammals, is described. Thus, cyclization of 5-bromo-2-[(2-chlorophenyl)methyl-N-valeryl]amino-3-nitrobenzoic acid (preparation given) in the presence of sodium bicarbonate solution containing sodium hydrosulfite at Ph 7.1 followed by acidic workup gave title compound, 5-bromo-2-butyl-1-(2-chlorophenyl)methyl-1H-benzimidazole-7-carboxylic acid. The pharmaceutical compns. of some of the compds. prepared is given.

IT **138993-09-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses).

(preparation of, as angiotensin II receptor antagonist)
RN 138993-09-6 CAPLUS
CN 1H-Benzimidazole-5,7-dicarboxylic acid, 2-butyl-1-[(2-chlorophenyl)methyl]- (9CI) (CA INDEX NAME)

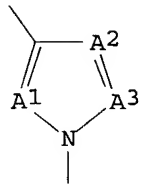
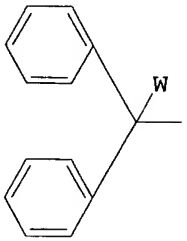
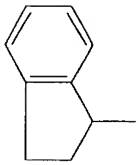


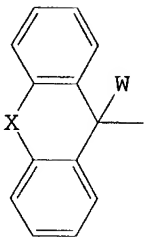
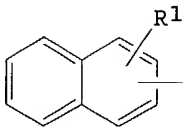

L6 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:656180 CAPLUS
DOCUMENT NUMBER: 115:256180
TITLE: Preparation of α-hexyl-4-(benzoylamino)-1H-imidazole-1-acetic acid, its derivatives, and analogs as angiotensin II antagonists
INVENTOR(S): Lifer, Sherryl L.; Marshall, Winston S.; Mohamadi, Fariborz; Reel, Jon K.; Simon, Richard L.; Steinberg, Mitchell I.; Whitesitt, Celia A.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA
SOURCE: Can. Pat. Appl., 79 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

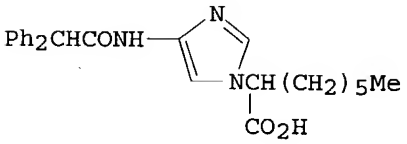
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CA 2030961 | AA | 19910531 | CA 1990-2030961 | 19901127 <-- |
| US 5073566 | A | 19911217 | US 1989-444456 | 19891130 <-- |
| EP 438869 | A1 | 19910731 | EP 1990-312913 | 19901128 <-- |
| EP 438869 | B1 | 19941214 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| ES 2064665 | T3 | 19950201 | ES 1990-312913 | 19901128 <-- |
| JP 03193745 | A2 | 19910823 | JP 1990-336864 | 19901129 <-- |
| JP 2935740 | B2 | 19990816 | | |
| US 5312936 | A | 19940517 | US 1991-761127 | 19910917 <-- |
| US 5571925 | A | 19961105 | US 1994-183685 | 19940119 <-- |
| US 5563278 | A | 19961008 | US 1995-453537 | 19950530 <-- |

PRIORITY APPLN. INFO.: US 1989-444456 19891130
US 1989-444465 19891130
US 1991-761127 19910917
US 1994-183685 19940119

OTHER SOURCE(S): MARPAT 115:256180
GI

Q=  Q1=  Q2= 

Q3=  Q4= 

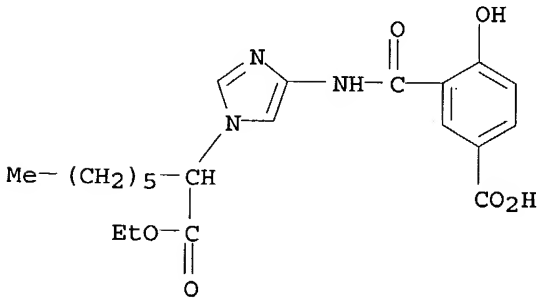


II


AB ArZGCHR1R2 [I; G = phenylene, bivalent 5-membered heterocyclic ring Q; Ar = substituted Ph, aromatic residue Q1-Q4; R1 = (CH2)nR3; R2 = C4-7 alkyl; Z = CO, CONH, NHCO, CH2CONH, O, NH, CH2, bond; R3 = HO, HO2C, 5-tetrazolyl; R4 = H, HO, halo, NO2, amino, Me, AcNH, MeSO2NH; A1-A3 = N, CH; W = Me, Et, HO; X = bond, O; n = 0-4] or their pharmaceutically acceptable salts or solvates, useful for **treating** congestive **heart failure** and angiotensin-induced hypertension, were prepared A solution of 41.8 g 4-nitroimidazole in DMF was refluxed 1 h with a suspension of NaH in DMF, the mixture was **treated** by 92 g Me(CH2)5CHBrCO2Et in DMF, and the whole refluxed for 2 h to give 10.40 g Et 4-nitro-α-hexyl-1H-imidazole-1-acetate. Hydrogenation of the latter (5.9 g) over Pd/C in EtOH gave 5.3 g 4-amino analog which (750 mg) was coupled with Ph2CHCO2H in the presence of carbonyldiimidazole in DMF to give 250 mg title compound (II·HCl). The latter at 10-5 M (test form unspecified) gave 80% inhibition of binding of 125I-angiotensin II to rat adrenal membranes. Formulations containing I are given.

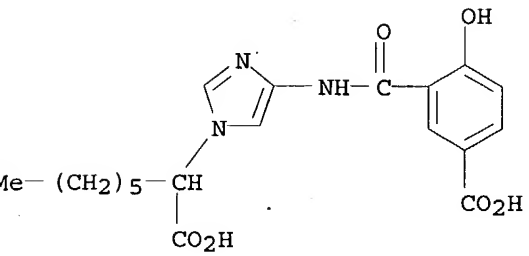

IT **137417-53-9P 137417-72-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as angiotensin II antagonist)

RN 137417-53-9 CAPLUS
CN 1H-Imidazole-1-acetic acid, 4-[(5-carboxy-2-hydroxybenzoyl)amino]-α-hexyl-, α-ethyl ester (9CI) (CA INDEX NAME)



RN 137417-72-2 CAPLUS
CN 1H-Imidazole-1-acetic acid, 4-[(5-carboxy-2-hydroxybenzoyl)amino]-α-

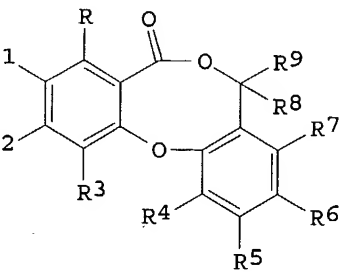
hexyl- (9CI) (CA INDEX NAME)



L6 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:428987 CAPLUS
DOCUMENT NUMBER: 115:28987
TITLE: Cardioactive dibenzo[1,5]dioxocin-5-one derivatives
INVENTOR(S): Frobel, Klaus; Lenfers, Jan Bernd; Fey, Peter; Knorr, Andreas; Stasch, Johannes Peter; Mueller, Hartwig; Bischoff, Erwin; Dellweg, Hans Georg
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Ger. Offen., 60 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 3919255 | A1 | 19901220 | DE 1989-3919255 | 19890613 <-- |
| US 5089487 | A | 19920218 | US 1990-528667 | 19900524 <-- |
| AU 9056008 | A1 | 19901220 | AU 1990-56008 | 19900528 <-- |
| AU 632578 | B2 | 19930107 | | |
| NO 9002400 | A | 19901214 | NO 1990-2400 | 19900530 <-- |
| NO 175745 | B | 19940822 | | |
| NO 175745 | C | 19941130 | | |
| EP 411268 | A2 | 19910206 | EP 1990-110336 | 19900531 <-- |
| EP 411268 | A3 | 19910703 | | |
| EP 411268 | B1 | 19950419 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| AT 121396 | E | 19950515 | AT 1990-110336 | 19900531 <-- |
| ES 2072332 | T3 | 19950716 | ES 1990-110336 | 19900531 <-- |
| CA 2018659 | AA | 19901213 | CA 1990-2018659 | 19900611 <-- |
| DD 298423 | A5 | 19920220 | DD 1990-341537 | 19900611 <-- |
| HU 54136 | A2 | 19910128 | HU 1990-3811 | 19900612 <-- |
| JP 03024073 | A2 | 19910201 | JP 1990-151794 | 19900612 <-- |
| ZA 9004524 | A | 19910424 | ZA 1990-4524 | 19900612 <-- |
| CN 1048041 | A | 19901226 | CN 1990-104489 | 19900613 <-- |

PRIORITY APPLN. INFO.: DE 1989-3919255 19890613
OTHER SOURCE(S): MARPAT 115:28987
GI



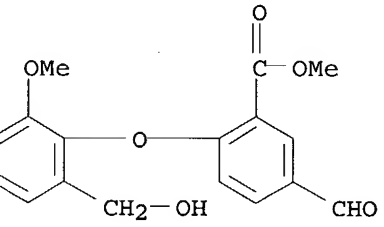
I

AB Penicillide derivs. I (R-R7 = H, (un)substituted alkyl, alkenyl, alkynyl; R8, R9 = H, (un)substituted alkyl] were prepared for use as antihypertensives, antiarrhythmics, and in the **treatment** of cardiac insufficiency (no data). Thus, I (R = R2 = R3 = R5-R9 = H, R1 = CHO, R4 = OMe) was obtained by alkoxylating 2,5-Br[(MeO)2CH]C6H3CO2Me with 2-methoxy-6-(2-tetrahydropyranyloxymethyl)phenol, ether cleavage, hydrolysis, and lactonization. Many I were prepared from penicillide.

IT **134563-73-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ester hydrolysis of)

RN 134563-73-8 CAPLUS

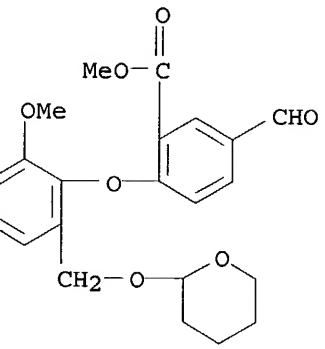
CN Benzoic acid, 5-formyl-2-[2-(hydroxymethyl)-6-methoxyphenoxy]-, methyl ester (9CI) (CA INDEX NAME)




IT **134563-70-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and ether cleavage of)

RN 134563-70-5 CAPLUS

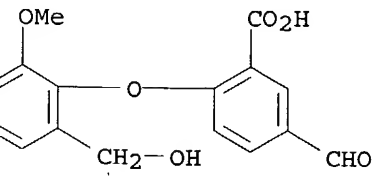
CN Benzoic acid, 5-formyl-2-[2-methoxy-6-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)




T **134563-81-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and lactonization of)

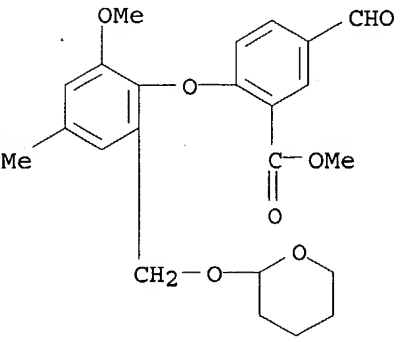
N 134563-81-8 CAPLUS

N Benzoic acid, 5-formyl-2-[2-(hydroxymethyl)-6-methoxyphenoxy]- (9CI) (CA INDEX NAME)




T **134563-71-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of)
RN 134563-71-6 CAPLUS
CN Benzoic acid, 5-formyl-2-[2-methoxy-4-methyl-6-[[(tetrahydro-2H-pyran-2-yl)oxy]methyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)




L6 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:228897 CAPLUS
DOCUMENT NUMBER: 114:228897
TITLE: Preparation of saccharin derivatives useful as proteolytic enzyme inhibitors.
INVENTOR(S): Dunlap, Richard Paul; Boaz, Neil Warren; Mura, Albert Joseph; Hlasta, Dennis John
PATENT ASSIGNEE(S): Sterling Drug Inc., USA
SOURCE: PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9013549 | A1 | 19901115 | WO 1990-US2434 | 19900501 <-- |
| W: AU, FI, JP, KR, NO | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE | | | | |
| CA 1336960 | A1 | 19950912 | CA 1989-611223 | 19890913 <-- |
| CA 1340252 | A1 | 19981215 | CA 1989-611220 | 19890913 <-- |
| AU 9056649 | A1 | 19901129 | AU 1990-56649 | 19900501 <-- |
| AU 637614 | B2 | 19930603 | | |
| EP 471756 | A1 | 19920226 | EP 1990-907695 | 19900501 <-- |
| EP 471756 | B1 | 19971029 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE | | | | |
| JP 04507095 | T2 | 19921210 | JP 1990-507810 | 19900501 <-- |
| AT 159720 | E | 19971115 | AT 1990-907695 | 19900501 <-- |
| ES 2110414 | T3 | 19980216 | ES 1990-907695 | 19900501 <-- |
| IL 94278 | A1 | 19950330 | IL 1990-94278 | 19900603 <-- |
| DD 297644 | A5 | 19920116 | DD 1990-343934 | 19900910 <-- |
| NO 9104217 | A | 19911028 | NO 1991-4217 | 19911028 <-- |
| US 5371074 | A | 19941206 | US 1993-67637 | 19930524 <-- |
| US 5380737 | A | 19950110 | US 1993-113508 | 19930827 <-- |
| US 5650422 | A | 19970722 | US 1994-270964 | 19940705 <-- |
| US 5464852 | A | 19951107 | US 1994-289113 | 19940811 <-- |
| FI 9404967 | A | 19941021 | FI 1994-4967 | 19941021 <-- |
| US 5578623 | A | 19961126 | US 1995-445240 | 19950519 <-- |
| US 5596012 | A | 19970121 | US 1995-449152 | 19950524 <-- |
| FI 9600488 | A | 19960202 | FI 1996-488 | 19960202 <-- |
| FI 9600489 | A | 19960202 | FI 1996-489 | 19960202 <-- |
| US 5773456 | A | 19980630 | US 1996-719216 | 19960925 <-- |
| US 5874432 | A | 19990223 | US 1997-803297 | 19970220 <-- |

| PRIORITY APPLN. INFO.: | | | |
|---|---|---|---|
| | US 1989-347125 | A | 19890504 |
| | US 1989-347126 | A | 19890504 |
| | US 1990-514920 | B2 | 19900426 |
| | WO 1990-US2434 | A | 19900501 |

| | | |
|---|---|---|
| US 1990-608068 | B2 | 19901101 |
| US 1991-782016 | A | 19911024 |
| FI 1991-5093 | A | 19911029 |
| US 1991-793033 | A3 | 19911115 |
| US 1991-793035 | B1 | 19911115 |
| US 1993-67637 | A3 | 19930524 |
| US 1993-113508 | A3 | 19930827 |
| US 1994-270964 | B3 | 19940705 |
| US 1994-289113 | A3 | 19940811 |
| FI 1994-4967 | A | 19941021 |
| US 1995-445240 | A3 | 19950519 |

OTHER SOURCE(S): MARPAT 114:228897

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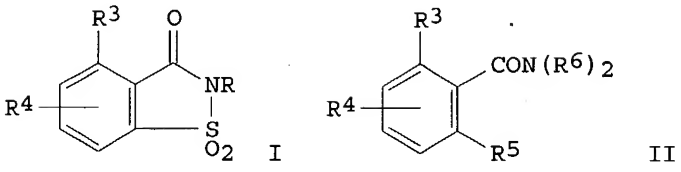


I II

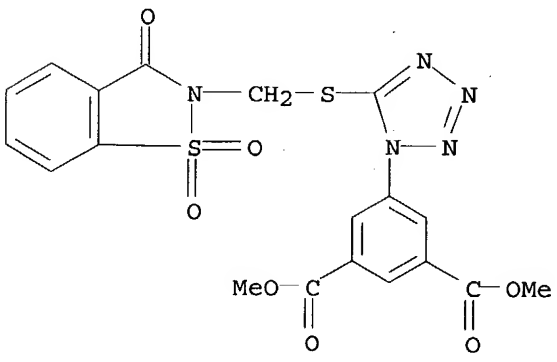
AB Saccharin derivs. [I; R = (CH:CH)mCHR2LnR1; L = O, S, SO, SO2; m, n = 0, 1; R1 = halo, alkanoyl, 1-oxophenalenyl, (substituted) Ph or heterocyclyl; R2 = H, carboalkoxy, Ph, PhS; R3 = H, halo, primary or secondary alkyl, alkoxy, carboalkoxy, Ph, fluoroalkyl, alkenyl, cyano; R4 = H, or 1 or 2 substituents selected from halo, cyano, NO2, (substituted) NH2, SO2NH2, OH, CHO, CH2OH, (polyhalo)alkyl, alkylsulfonyl, cycloalkyl, etc.], protease inhibitors useful in the **treatment** of, e.g., emphysema, **rheumatoid arthritis**, and pancreatitis, are prepared by, e.g., (1) reaction of I (R = CH2X; X = halo) with a LnR1 alkali metal salt; (2) reaction of I (R = H) with X1CHR2LnR1(X1 = halo); and (3) oxidation of I [R = CH(SPh)CH2CH2LnR1] to the sulfoxide followed by elimination to give I (m = 1, R2 = H). I (R = H) are prepared by lithiation of benzamides II (R3 = R5 = H, R6 = alkyl) followed by **treatment** with R3X2 (X2 = halo), lithiation of the resulting II (R3 = primary or secondary alkyl; R4,R6 = same as above) followed by reaction with SO2 and then a H2NOSO3H alkali metal salt, and heating the resulting I (R3, R6 = same above, R5 = SO2NH2) for cyclization. Thus, diazotization of Me 6-methylanthranilate with NaNO2 in concentrated HCl and AcOH followed by reaction with CuCl2.2H2O and SO3 gave Me 6-methyl-2-(chlorosulfonyl)anthranilate which was stirred with aqueous NH4OH to give 12% 4-methylsaccharin. Hydroxymethylation of the latter with HCHO in EtOH followed by acetylation with Ac2O in the presence of concentrated H2SO4 gave 73% I (R = CH2OAc, R3 = Me, R4 = H). A total of 124 I were prepared which in vitro inhibited elastase with Ki ≥ 0.3 nM.

IT **133743-27-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as protease inhibitor)

RN 133743-27-8 CAPLUS

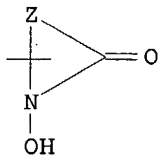
CN 1,3-Benzenedicarboxylic acid, 5-[5-[[(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)methyl]thio]-1H-tetrazol-1-yl]-, dimethyl ester (9CI) (CA INDEX NAME)



L6 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:515323 CAPLUS
DOCUMENT NUMBER: 113:115323
TITLE: Preparation of nonsteroidal antiinflammatory drugs
INVENTOR(S): Jackson, William Paul; Pettipher, Eric Roy
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9001929 | A1 | 19900308 | WO 1989-GB992 | 19890825 <-- |
| W: JP, US | | | | |
| RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| PRIORITY APPLN. INFO.: | | | GB 1988-20185 | 19880825 |
| OTHER SOURCE(S): | MARPAT 113:115323 | | | |

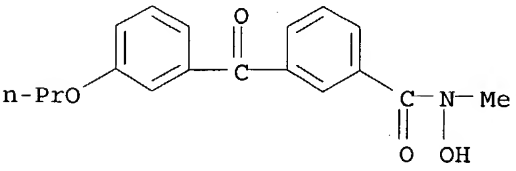
GI

Q1= 

AB Ar(LAr1)q(X)k(Y)pQ [I; k, p, q = 0.1; provided that when k = 1, p = 1; Ar = (un)substituted furyl, thienyl 1,1-dioxide, pyrryl, pyridyl, benzofuryl, Ph, etc.: L = (CH2)r, O, CH2O, CH2S, OCH2, CONH, NHCO, CO, CH2NH; r = 1-4; Ar1 = (un)substituted phenylene, thienylene, or pyridylene; X = O, S, CO; Y = C1-10 alkylene or alkenylene; Q = Q1, (CO)nN(OR1)(CO)mR2; m, n = 0, 1; when n = 1, m = 0 and R1,R2 = H, C1-4 alkyl or R2 = C5-7 cycloalkyl; when n = 0, m = 1, R1 = H, C1-4 alkyl, any one of Ar, alkanoyl, or (un)substituted CONH2 and R2 = H, C1-4 alkyl, NH2, C1-4 mono- or dialkylamino, anilino, etc.; Z = C2-5 alkylene optionally interrupted by a hetero atom], useful for **treatment** of arthritis, e.g., **rheumatoid arthritis**, rheumatoid spondylitis, **osteoarthritis**, gouty arthritis, or reactive arthritis, are prepared Thus, a solution of HSCH2CO2Me in THF was added dropwise to 1-(1-naphthyl)-2-nitroethene and Et3N in THF and after stirring 30 min at room temperature, the mixture was evaporated in vacuo, dissolved in saturated aqueous NH4Cl in 95 % EtOH, and then stirred 30 min with Zn powder to give 5,6-dihydro-1-hydroxy-5-(1-naphthyl)-1,4-thiazine-3(2H,4H)-one. A total of 88 I were prepared N-(3-Phenoxycinnamyl)acetohydroxamic acid (II) reduced the ovalbumin-induced swelling (arthritis) in the right knee joint of rabbits immunized with ovalbumin in Freund's complete adjuvant and II in combination with indomethacin, up to 51 %. Tablets and an injection solution containing II were formulated.

IT **106328-20-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiarthritic)

RN 106328-20-5 CAPLUS
CN Benzamide, N-hydroxy-N-methyl-3-(3-propoxybenzoyl)- (9CI) (CA INDEX NAME)

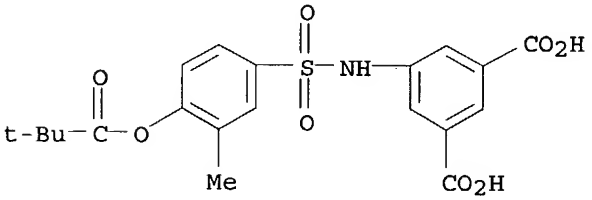


L6 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:514810 CAPLUS
DOCUMENT NUMBER: 113:114810
TITLE: Preparation of p-substituted phenyl ester of pivalic acid as elastase inhibitors and pharmaceutical compositions
INVENTOR(S): Imaki, Katsuhiro; Arai, Yoshinobu; Okegawa, Tadao
PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 91 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 347168 | A1 | 19891220 | EP 1989-305959 | 19890613 <-- |
| EP 347168 | B1 | 19930901 | | |
| R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| US 5017610 | A | 19910521 | US 1989-364994 | 19890612 <-- |
| CA 1340191 | A1 | 19981215 | CA 1989-602530 | 19890612 <-- |
| JP 03020253 | A2 | 19910129 | JP 1989-148479 | 19890613 <-- |
| JP 05081586 | B4 | 19931115 | | |
| AT 93843 | E | 19930915 | AT 1989-305959 | 19890613 <-- |
| ES 2059752 | T3 | 19941116 | ES 1989-305959 | 19890613 <-- |
| JP 06179645 | A2 | 19940628 | JP 1992-241380 | 19920819 <-- |
| JP 06094450 | B4 | 19941124 | | |
| US 5336681 | A | 19940809 | US 1992-960301 | 19921013 <-- |
| US 5403850 | A | 19950404 | US 1994-235856 | 19940429 <-- |

PRIORITY APPLN. INFO.:
JP 1988-145450 19880613
JP 1989-53541 19890306
US 1989-364994 19890612
EP 1989-305959 19890613
US 1991-681364 19910408
US 1992-960301 19921013

OTHER SOURCE(S): MARPAT 113:114810
GI For diagram(s), see printed CA Issue.
AB The title esters [I; Y = SO2, CO; R1,R2 = H, (substituted) C1-16 alkyl, Q (wherein X = bond, SO2, C1-4 alkylene optionally substituted with CO2H or CO2CH2Ph; ring A is carbocyclic or heterocyclic; R4 = H, C1-8 alkyl, C1-4 alkoxy, etc.; n = 1-5), R1R2N = (substituted) heterocyclic; R3 = H, OH, C1-6 alkyl, halo, C1-4 alkoxy, C2-5 acyloxy, m = 1-4], useful as elastase inhibitors in **treating** or preventing pulmonary emphysema, atherosclerosis, and **rheumatoid arthritis**, are prepared Pivaloyl chloride (0.5 mL) was added to a solution of II (R = H) (preparation given) in Et3N-CH2Cl2 under cooling and the solution was stirred 1 h at room temperature to give 510 mg II (R = pivaloyl), which showed elastase inhibition at 0.031 μM. Also prepared were 134 addnl. I.
IT **127373-55-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as elastase inhibitor)
RN 127373-55-1 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[[4-(2,2-dimethyl-1-oxopropoxy)-3-methylphenyl]sulfonyl]amino]- (9CI) (CA INDEX NAME)



L6 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:156489 CAPLUS
DOCUMENT NUMBER: 106:156489
TITLE: Bis(6-oxopyridazinyl)benzene derivatives as drugs
INVENTOR(S): Prain, Hunter Douglas; Warrington, Brian Herbert
PATENT ASSIGNEE(S): Smith Kline and French Laboratories Ltd., UK
SOURCE: Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 208517 | A2 | 19870114 | EP 1986-305187 | 19860704 <-- |
| EP 208517 | A3 | 19880323 | | |
| EP 208517 | B1 | 19900912 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | | | | |
| IL 79280 | A1 | 19900712 | IL 1986-79280 | 19860630 <-- |
| US 4904664 | A | 19900227 | US 1986-880849 | 19860701 <-- |
| AU 8659488 | A1 | 19870108 | AU 1986-59488 | 19860702 <-- |
| AU 580677 | B2 | 19890127 | | |
| DK 8603169 | A | 19870106 | DK 1986-3169 | 19860703 <-- |
| ZA 8604954 | A | 19870225 | ZA 1986-4954 | 19860703 <-- |
| FI 8602840 | A | 19870106 | FI 1986-2840 | 19860704 <-- |
| NO 8602723 | A | 19870106 | NO 1986-2723 | 19860704 <-- |
| JP 62012765 | A2 | 19870121 | JP 1986-158634 | 19860704 <-- |
| JP 05086951 | B4 | 19931214 | | |
| HU 41393 | A2 | 19870428 | HU 1986-2821 | 19860704 <-- |
| ES 2000209 | A6 | 19880116 | ES 1986-129 | 19860704 <-- |
| AT 56440 | E | 19900915 | AT 1986-305187 | 19860704 <-- |
| CN 86105663 | A | 19870121 | CN 1986-105663 | 19860705 <-- |
| PRIORITY APPLN. INFO.: | | | GB 1985-17051 | 19850705 |
| | | | GB 1986-6853 | 19860320 |
| | | | EP 1986-305187 | 19860704 |

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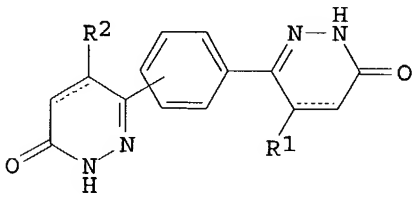

I

AB The title compds. (I; R1, R2 = H, Me; dotted lines = optional double bonds; the benzene ring is m- or p-substituted) were prepared as phosphodiesterase inhibitors, useful in **treating** congestive **heart failure**. C6H4(COMe)2-1,4 condensed with HCOCO2H to give 1,4-(HO2CCH:CHCO)2C6H4 which cyclocondensed with N2H4 to give I (R1 = R2 = H, dotted line = bond, p-substituted) (II). In cats 0.04 μmol II/kg increased left ventricular contractility 50%. Capsules were prepared containing active ingredient 0.5, soya lecithin/soybean oil 90.45, hydrogenated vegetable oil/beeswax 9.05%.

IT **107549-79-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclocondensation of, with piperazine)

RN 107549-79-1 CAPLUS
CN 2-Butenoic acid, 4,4'-(1,3-phenylene)bis[4-oxo- (9CI) (CA INDEX NAME)